

Epilepsy: classification

The basic classification of epilepsy has changed in recent years. The new basic seizure classification is based on 3 key features:

- 1. Where seizures begin in the brain
- 2. Level of awareness during a seizure (important as can affect safety during seizure)
- 3. Other features of seizures

Focal seizures

- previously termed partial seizures
- these start in a specific area, on one side of the brain
- the level of awareness can vary in focal seizures. The terms focal aware (previously termed 'simple partial'), focal impaired awareness (previously termed 'complex partial') and awareness unknown are used to further describe focal seizures
- further to this, focal seizures can be classified as being motor (e.g. Jacksonian march), non-motor (e.g. déjà vu, jamais vu;) or having other features such as aura

Generalised

- these engage or involve networks on both sides of the brain at the onset
- consciousness lost immediately. The level of awareness in the above classification is therefore not needed, as all patients lose consciousness
- generalised seizures can be further subdivided into motor (e.g. tonic-clonic) and non-motor (e.g. absence)
- specific types include:
 - → tonic-clonic (grand mal)
 - → tonic
 - → clonic
 - → typical absence (petit mal)
 - → myoclonic: brief, rapid muscle jerks
 - → atonic

Unknown onset

- this termed is reserved for when the origin of the seizure is unknown

Focal to bilateral seizure

- starts on one side of the brain in a specific area before spreading to both lobes
- previously termed secondary generalized seizures

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Epilepsy in children: syndromes

Infantile spasms (West's syndrome)

- brief spasms beginning in first few (4-6) months of life; M>F
- 1. Flexion of head, trunk, limbs → extension of arms (Salaam attack); last 1-2 secs, repeat up to 50 times
- 2. Progressive mental handicap
- 3. EEG: hypsarrhythmia
- usually 2nd to serious neurological abnormality (e.g. TS, encephalitis, birth asphyxia) or may be cryptogenic
- poor prognosis
- vigabatrin/steroids

Typical (petit mal) absence seizures

- onset 4-8 yrs
- duration few-30 secs; no warning, quick recovery; often many per day
- EEG: 3Hz generalized, symmetrical
- sodium valproate, ethosuximide
- good prognosis: 90-95% become seizure free in adolescence

Lennox-Gastaut syndrome

- may be extension of infantile spasms (50% have hx)
- onset 1-5 yrs
- atypical absences, falls, jerks
- 90% moderate-severe mental handicap
- EEG: slow spike
- ketogenic diet may help

Benign rolandic epilepsy

- most common in childhood, M>F
- paraesthesia (e.g. unilateral face), usually on waking up

Juvenile myoclonic epilepsy (Janz syndrome)

- onset: teens; F:M = 2:1
- 1. Infrequent generalized seizures, often in morning
- 2. Daytime absences
- 3. Sudden, shock like myoclonic seizure
- usually good response to sodium valproate

Neonatal period - try vitamin B6

- 2nd: hypoglycaemia, meningitis, head trauma
 - pyridoxine dependency (AR, IV B6)
 - benign familial neonatal seizures (AD)
 - benign neonatal convulsions (5th day)
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Epilepsy: localising features of focal seizures

Location	Typical seizure type
Temporal lobe (HEAD)	Hallucinations (auditory/gustatory/olfactory), Epigastric rising/Emotional, Automatisms (lip smacking/grabbing), Deja vu/Dysphasia post-ictal)
Frontal lobe (motor)	Head/leg movements , posturing, post-ictal weakness
Parietal lobe (sensory)	Paraesthesia
Occipital lobe (visual)	Floaters/flashes

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Cataplexy

Cataplexy describes the sudden and transient loss of muscular tone caused by strong emotion (e.g. laughter, being frightened). Around two-thirds of patients with narcolepsy have cataplexy.

Features range from buckling knees to collapse.

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Narcolepsy

Overview

- associated with HLA-DR2
- it is associated with low levels of orexin (hypocretin), a protein which is responsible for controlling appetite and sleep patterns
- early onset of REM sleep

Features

- typical onset in teenage years
- hypersomnolence
- cataplexy (sudden loss of muscle tone often triggered by emotion)
- sleep paralysis
- vivid hallucinations on going to sleep or waking up

Investigation

- multiple sleep latency EEG

Next question

Absence seizures

Absence seizures (petit mal) are a form of generalised epilepsy that is mostly seen in children. The typical age of onset of 3-10 years old and girls are affected twice as commonly as boys

Features

- absences last a few seconds and are associated with a quick recovery
- seizures may be provoked by hyperventilation or stress
- the child is usually unaware of the seizure
- they may occur many times a day
- EEG: bilateral, symmetrical 3Hz spike and wave pattern

Management

- sodium valproate and ethosuximide are first-line treatment
- good prognosis - 90-95% become seizure free in adolescence

Next question >

Status epilepticus

This is a medical emergency. The priority is termination of seizure activity, which if prolonged will lead to irreversible brain damage. First-line drugs are benzodiazepines such as diazepam or lorazepam. If ineffective within 10 minutes it is appropriate to start a second-line agent such as phenytoin, sodium valproate, levetiracetam, or phenobarbital. If no response within 30 minutes from onset, then the best way to achieve rapid control of seizure activity is induction of general anaesthesia.

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Epilepsy: pregnancy and breast feeding

The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus. All women thinking about becoming pregnant should be advised to take folic acid 5mg per day well before pregnancy to minimise the risk of neural tube defects. Around 1-2% of newborns born to non-epileptic mothers have congenital defects. This rises to 3-4% if the mother takes antiepileptic medication.

Other points

- aim for monotherapy
- there is no indication to monitor antiepileptic drug levels
- sodium valproate: associated with neural tube defects
- carbamazepine: often considered the least teratogenic of the older antiepileptics
- phenytoin: associated with cleft palate
- lamotrigine: studies to date suggest the rate of congenital malformations may be low. The dose of lamotrigine may need to be increased in pregnancy

Breast feeding is generally considered safe for mothers taking antiepileptics with the possible exception of the barbiturates

It is advised that pregnant women taking phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn

Sodium valproate

The November 2013 issue of the Drug Safety Update also carried a warning about new evidence showing a significant risk of neurodevelopmental delay in children following maternal use of sodium valproate.

The update concludes that sodium valproate should not be used during pregnancy and in women of childbearing age unless clearly necessary. Women of childbearing age should not start treatment without specialist neurological or psychiatric advice.

Next question >

Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

Focal** seizures

- carbamazepine or lamotrigine
- second line: levetiracetam, oxcarbazepine or sodium valproate

*carbamazepine may actually exacerbate absence seizure

** the preferred term for partial seizures

Phenytoin

Phenytoin is used to in the management of seizures.

Mechanism of action

- binds to sodium channels increasing their refractory period

Adverse effects

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute

- initially: dizziness, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic

- common: gingival hyperplasia (secondary to increased expression of platelet derived growth factor, PDGF), hirsutism, coarsening of facial features, drowsiness
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic

- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture*
- aplastic anaemia
- drug-induced lupus

Teratogenic

- associated with cleft palate and congenital heart disease

Monitoring

Phenytoin levels do not need to be monitored routinely but **trough levels, immediately before dose** should be checked if:

- adjustment of phenytoin dose
- suspected toxicity
- detection of non-adherence to the prescribed medication

*although not listed in the BNF

Sodium valproate

Sodium valproate is used in the management of epilepsy and is first line therapy for generalised seizures. It works by increasing GABA activity.

Adverse effects

- gastrointestinal: nausea
- increased appetite and weight gain
- alopecia: regrowth may be curly
- ataxia
- tremor
- hepatitis
- pancreatitis
- thrombocytopaenia
- teratogenic
- hyponatraemia

The screenshot shows a medical application interface. On the left, a sidebar contains a 'Questions' section with a list of topics: 'A young man', 'examina...', 'Extradu...', 'Multipl...', 'Guillain', and 'Cavern...'. The main content area displays a question about Lamotrigine. The question text is: 'Lamotrigine is an antiepileptic used second-line for a variety of generalised and partial seizures.' Below the question, there are two sections: 'Mechanism of action' and 'Adverse effects'. The 'Mechanism of action' section lists 'sodium channel blocker'. The 'Adverse effects' section lists 'Stevens-Johnson syndrome'. The interface includes a top toolbar with various icons and a bottom toolbar with more icons. A close button (X) is located in the top right corner of the question card.

Lamotrigine

Lamotrigine is an antiepileptic used second-line for a variety of generalised and partial seizures.

Mechanism of action

- sodium channel blocker

Adverse effects

- Stevens-Johnson syndrome

Carbamazepine

Carbamazepine is chemically similar to the tricyclic antidepressant drugs. It is most commonly used in the treatment of epilepsy, particularly partial seizures, where carbamazepine remains a first-line medication. Other uses include

- neuropathic pain (e.g. trigeminal neuralgia, diabetic neuropathy)
- bipolar disorder

Mechanism of action

- binds to sodium channels increases their refractory period

Adverse effects

- P450 enzyme inducer
- dizziness and ataxia
- drowsiness
- headache
- visual disturbances (especially diplopia)
- Steven-Johnson syndrome
- leucopenia and agranulocytosis
- syndrome of inappropriate ADH secretion



Multiple system atrophy

Shy-Drager syndrome is a type of multiple system atrophy

Features

- parkinsonism
- autonomic disturbance (atonic bladder, postural hypotension)
- cerebellar signs



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Aphasia

The table below lists the major types of aphasia. Remember that dysarthria is different and refers to a motor speech disorder.

Type of aphasia	Notes
Wernicke's (receptive) aphasia	Due to a lesion of the superior temporal gyrus This area 'forms' the speech before 'sending it' to Broca's area. Lesions result in sentences that make no sense, word substitution and neologisms but speech remains fluent Comprehension is impaired
Broca's (expressive) aphasia	Due to a lesion of the inferior frontal gyrus Speech is non-fluent, laboured, and halting Comprehension is normal
Conduction aphasia	Classically due to a stroke affecting the arcuate fasciculus - the connection between Wernicke's and Broca's area Speech is fluent but repetition is poor. Aware of the errors they are making Comprehension is normal
Global aphasia	Large lesion affecting all 3 of the above areas resulting in severe expressive and receptive aphasia

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Broca's dysphasia: speech non-fluent, comprehension normal, repetition good

Type of dysphasia	Lesion location	Speech	Comprehension	Repetition
Wernicke's (receptive) dysphasia	Superior temporal gyrus	Fluent	Abnormal	Good
Conduction (associative) dysphasia	Arcuate fasciculus	Fluent	Abnormal	Poor
Broca's (expressive) dysphasia	Inferior frontal gyrus	Non-fluent	Normal	Good

The middle cerebral artery supplies medial part of cerebrum containing frontal lobe and medial temporal lobe and therefore supplies Broca's area in the inferior frontal gyrus.





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Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

Cutaneous features

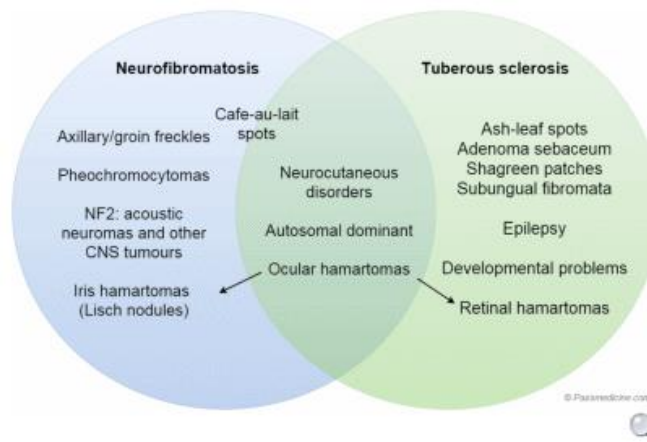
- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum (angiofibromas): butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots* may be seen

Neurological features

- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

Also

- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata
- lymphangioliomyomatosis: multiple lung cysts



Comparison of neurofibromatosis and tuberous sclerosis. Note that whilst they are both autosomal dominant neurocutaneous disorders there is little overlap otherwise

*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

Neurofibromatosis

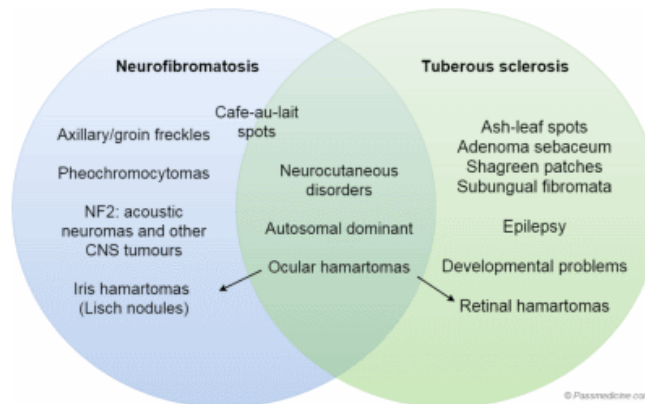
There are two types of neurofibromatosis, NF1 and NF2. Both are inherited in an autosomal dominant fashion

NF1 is also known as von Recklinghausen's syndrome. It is caused by a gene mutation on chromosome 17 which encodes neurofibromin and affects around 1 in 4,000

NF2 is caused by gene mutation on chromosome 22 and affects around 1 in 100,000

Features

NF1	NF2
Café-au-lait spots (≥ 6, 15 mm in diameter) Axillary/groin freckles Peripheral neurofibromas Iris hamatomas (Lisch nodules) in $> 90\%$ Scoliosis Pheochromocytomas	Bilateral acoustic neuromas Multiple intracranial schwannomas, meningiomas and ependymomas



Comparison of neurofibromatosis and tuberous sclerosis. Note that whilst they are both autosomal dominant neurocutaneous disorders there is little overlap otherwise

Von Hippel-Lindau syndrome

Von Hippel-Lindau (VHL) syndrome is an autosomal dominant condition predisposing to neoplasia. It is due to an abnormality in the VHL gene located on short arm of chromosome 3

Features

- cerebellar haemangiomas
- retinal haemangiomas: vitreous haemorrhage
- renal cysts (premalignant)
- pheochromocytoma
- extra-renal cysts: epididymal, pancreatic, hepatic
- endolymphatic sac tumours



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CT scan showing a cerebellar haemangioma in a patient with Von Hippel-Lindau syndrome.

Reye's syndrome

Reye's syndrome is a severe, progressive encephalopathy affecting children that is accompanied by fatty infiltration of the liver, kidneys and pancreas. The aetiology of Reye's syndrome is not fully understood although there is a known association with aspirin use and a viral cause has been postulated

The peak incidence is 2 years of age, features include:

- may be history of preceding viral illness
- encephalopathy: confusion, seizures, cerebral oedema, coma
- fatty infiltration of the liver, kidneys and pancreas
- hypoglycaemia

Management is supportive

Although the prognosis has improved over recent years there is still a mortality rate of 15-25%.



Motor neuron disease: features



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Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

There are a number of clues which point towards a diagnosis of motor neuron disease:

- fasciculation
- the absence of sensory signs/symptoms*
- the mixture of lower motor neurone and upper motor neurone signs
- wasting of the small hand muscles/tibialis anterior is common

81 fact

Other features

- doesn't affect external ocular muscles
- no cerebellar signs
- abdominal reflexes are usually preserved and sphincter dysfunction if present is a late feature

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The diagnosis of motor neuron disease is clinical, but nerve conduction studies will show normal motor conduction and can help exclude a neuropathy. Electromyography shows a reduced number of action potentials with an increased amplitude. MRI is usually performed to exclude the differential diagnosis of cervical cord compression and myelopathy

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*vague sensory symptoms may occur early in the disease (e.g. limb pain) but 'never' sensory signs

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Motor neuron disease: types

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, primary lateral sclerosis, progressive muscular atrophy and progressive bulbar palsy. In some patients however, there is a combination of clinical patterns

Amyotrophic lateral sclerosis (50% of patients)

- typically LMN signs in arms and UMN signs in legs
- in familial cases the gene responsible lies on chromosome 21 and codes for superoxide dismutase

Primary lateral sclerosis

- UMN signs only

Progressive muscular atrophy

- LMN signs only
- affects distal muscles before proximal
- carries best prognosis

Progressive bulbar palsy

- palsy of the tongue, muscles of chewing/swallowing and facial muscles due to loss of function of brainstem motor nuclei
- carries worst prognosis

Next question >

Motor neuron disease: management

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

Riluzole

- prevents stimulation of glutamate receptors
- used mainly in amyotrophic lateral sclerosis
- prolongs life by about 3 months

Respiratory care

- non-invasive ventilation (usually BIPAP) is used at night
- studies have shown a survival benefit of around 7 months

Prognosis

- poor: 50% of patients die within 3 years

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[2016 Motor neurone disease: assessment and management](#)

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Guillain-Barre syndrome: features

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Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*).

The characteristic features of Guillain-Barre syndrome is progressive weakness of all four limbs. The weakness is classically ascending i.e. the lower extremities are affected first, however it tends to affect proximal muscles earlier than the distal ones. Sensory symptoms tend to be mild (e.g. distal paraesthesia) with very few sensory signs. Some patients experience back pain in the initial stages of the illness

Other features

- areflexia
- cranial nerve involvement e.g. diplopia
- autonomic involvement: e.g. urinary retention

Less common findings

- papilloedema: thought to be secondary to reduced CSF resorption

Guillain-Barre syndrome: management

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*).

Management

- plasma exchange
- IV immunoglobulins (IVIG): as effective as plasma exchange. No benefit in combining both treatments. IVIG may be easier to administer and tends to have fewer side-effects
- steroids and immunosuppressants have not been shown to be beneficial
- FVC regularly to monitor respiratory function

Prognosis

- 20% suffer permanent disability, 5% die

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Relevant to my revision >

Less relevant >

Dystrophinopathies

Overview

- X-linked recessive
- due to mutation in the gene encoding dystrophin, dystrophin gene on Xp21
- dystrophin is part of a large membrane associated protein in muscle which connects the muscle membrane to actin, part of the muscle cytoskeleton
- in Duchenne muscular dystrophy there is a frameshift mutation resulting in one or both of the binding sites are lost leading to a severe form
- in Becker muscular dystrophy there is a non-frameshift insertion in the dystrophin gene resulting in both binding sites being preserved leading to a milder form

Duchenne muscular dystrophy

- progressive proximal muscle weakness from 5 years
- calf pseudohypertrophy
- Gower's sign: child uses arms to stand up from a squatted position
- 30% of patients have intellectual impairment

Becker muscular dystrophy

- develops after the age of 10 years
- intellectual impairment much less common

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Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

Transient global amnesia

Overview

- presents with transient loss of memory function
- patients may appear anxious and repeatedly ask the same question
- patients have no recall of events after the attack
- aetiology is unknown, thought to be due to transient ischaemia to the thalamus (in particular the amygdala and hippocampus)

Dementia

Dementia is thought to affect over 700,000 people in the UK and accounts for a large amount of health and social care spending. The most common cause of dementia in the UK is Alzheimer's disease followed by vascular and Lewy body dementia. These conditions may coexist.

Features

- diagnosis can be difficult and is often delayed
- assessment tools include the Abbreviated mental test score (AMTS), 6-Item cognitive impairment test (6CIT), General practitioner assessment of cognition (GPCOG) and the mini-mental state examination (MMSE) is widely used. A MMSE score of 24 or less out of 30 suggests dementia

Management

- in primary care a blood screen is usually sent to exclude reversible causes (e.g. Hypothyroidism). NICE recommend the following tests: FBC, U&E, LFTs, calcium, glucose, TFTs, vitamin B12 and folate levels. Patients are now commonly referred on to old-age psychiatrists (sometimes working in 'memory clinics').
- in secondary care neuroimaging is performed* to exclude other reversible conditions (e.g. Subdural haematoma, normal pressure hydrocephalus) and help provide information on aetiology to guide prognosis and management

*in the 2011 NICE guidelines structural imaging was said to be essential in the investigation of dementia

Dementia: causes

Common causes

- Alzheimer's disease
- cerebrovascular disease: multi-infarct dementia (c. 10-20%)
- Lewy body dementia (c. 10-20%)

Rarer causes (c. 5% of cases)

- Huntington's
- CJD
- Pick's disease (atrophy of frontal and temporal lobes)
- HIV (50% of AIDS patients)

Important differentials, potentially treatable

- hypothyroidism, Addison's
- B12/folate/thiamine deficiency
- syphilis
- brain tumour
- normal pressure hydrocephalus
- subdural haematoma
- depression
- chronic drug use e.g. Alcohol, barbiturates

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Phenytoin may cause fever

Notes (1/1)

Frontotemporal lobar degeneration

Frontotemporal lobar degeneration (FTLD) is the third most common type of cortical dementia after Alzheimer's and Lewy body dementia.

There are three recognised types of FTLD

- Frontotemporal dementia (Pick's disease)
- Progressive non fluent aphasia (chronic progressive aphasia, CPA)
- Semantic dementia

Common features of frontotemporal lobar dementias

Onset before 65

Insidious onset

Relatively preserved memory and visuospatial skills

Personality change and social conduct problems

Pick's disease

This is the most common type and is characterised by personality change and impaired social conduct. Other common features include hyperorality, disinhibition, increased appetite, and perseveration behaviours.

Focal gyral atrophy with a knife-blade appearance is characteristic of Pick's disease.

Macroscopic changes seen in Pick's disease include:-

- Atrophy of the frontal and temporal lobes

Microscopic changes include:-

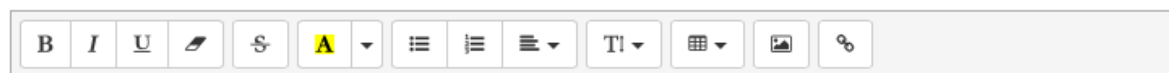
- Pick bodies - spherical aggregations of tau protein (silver-staining)
- Gliosis
- Neurofibrillary tangles
- Senile plaques

CPA

Here the chief factor is non fluent speech. They make short utterances that are agrammatic. Comprehension is relatively preserved.

Semantic dementia

Here the patient has a fluent progressive aphasia. The speech is fluent but empty and conveys little meaning. Unlike in Alzheimer's memory is better for recent rather than remote events.



Wernicke's encephalopathy

Wernicke's encephalopathy is a neuropsychiatric disorder caused by thiamine deficiency which is most commonly seen in alcoholics. Rarer causes include: persistent vomiting, stomach cancer, dietary deficiency. A classic triad of ophthalmoplegia/nystagmus, ataxia and confusion may occur. In Wernicke's encephalopathy petechial haemorrhages occur in a variety of structures in the brain including the mamillary bodies and ventricle walls

Features

- nystagmus (the most common ocular sign)
- ophthalmoplegia
- ataxia
- confusion, altered GCS
- peripheral sensory neuropathy

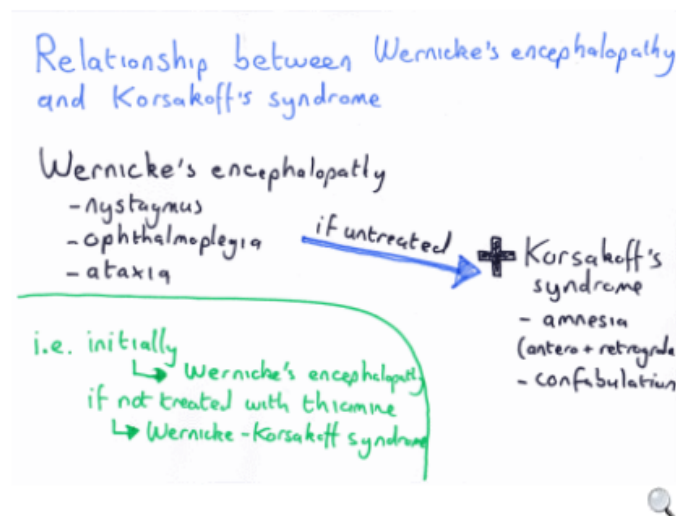
Investigations

- decreased red cell transketolase
- MRI

Treatment is with urgent replacement of thiamine

Relationship with Korsakoff syndrome

If not treated Korsakoff's syndrome may develop as well. This is termed Wernicke-Korsakoff syndrome and is characterised by the addition of antero- and retrograde amnesia and confabulation in addition to the above symptoms.





Alzheimer's disease



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Alzheimer's disease is a progressive degenerative disease of the brain accounting for the majority of dementia seen in the UK

Genetics

- most cases are sporadic
- 5% of cases are inherited as an autosomal dominant trait
- mutations in the amyloid precursor protein (chromosome 21), presenilin 1 (chromosome 14) and presenilin 2 (chromosome 1) genes are thought to cause the inherited form
- apolipoprotein E allele E4 - encodes a cholesterol transport protein

Pathological changes

- macroscopic: widespread cerebral atrophy, particularly involving the cortex and hippocampus
- microscopic: cortical plaques due to deposition of type A-Beta-amyloid protein and intraneuronal neurofibrillary tangles caused by abnormal aggregation of the tau protein
- biochemical: there is a deficit of acetylcholine from damage to an ascending forebrain projection

Neurofibrillary tangles

- paired helical filaments are partly made from a protein called tau
- in AD tau proteins are excessively phosphorylated

Management

- NICE now recommend the three acetylcholinesterase inhibitors (donepezil, galantamine and rivastigmine) as options for managing mild to moderate Alzheimer's disease
- memantine (a NMDA receptor antagonist) is reserved for patients with
 - moderate Alzheimer's who are intolerant of, or have a contraindication to, acetylcholinesterase inhibitors
 - severe Alzheimer's

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Parkinsonism

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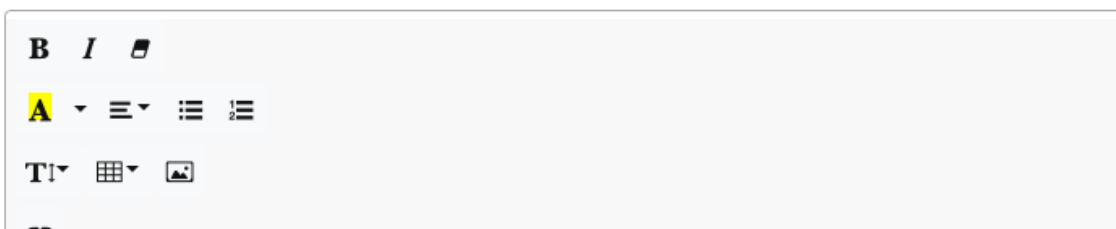
- Parkinson's disease
- drug-induced e.g. antipsychotics, metoclopramide - see below
- progressive supranuclear palsy
- multiple system atrophy
- Wilson's disease
- post-encephalitis
- dementia pugilistica (secondary to chronic head trauma e.g. boxing)
- toxins: carbon monoxide, MPTP

Drugs causing Parkinsonism

- phenothiazines: e.g. chlorpromazine, prochlorperazine
- butyrophenones: haloperidol, droperidol
- metoclopramide

Domperidone does not cross the blood-brain barrier and therefore does not cause extra-pyramidal side-effects

Next question >





Pass

Parkinson's disease: features



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Questi

Parkinson's disease is a progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra.. This results in a classic triad of features: bradykinesia, tremor and rigidity. The symptoms of Parkinson's disease are characteristically asymmetrical.

Tremor o

Epidemiology

- around twice as common in men
- mean age of diagnosis is 65 years

Gliolast

Normal

Von Hig

Parkins

Lewy b

Essenti

Bradykinesia

- poverty of movement also seen, sometimes referred to as hypokinesia
- short, shuffling steps with reduced arm swinging
- difficulty in initiating movement

Tremor

- most marked at rest, 3-5 Hz
- worse when stressed or tired
- typically 'pill-rolling', i.e. in the thumb and index finger

Rigidity

- lead pipe
- cogwheel: due to superimposed tremor

245 fac

Other characteristic features

- mask-like facies
- flexed posture
- micrographia
- drooling of saliva
- psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur
- impaired olfaction
- REM sleep behaviour disorder

Score f

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Parkins

Drug-induced parkinsonism has slightly different features to Parkinson's disease:

- motor symptoms are generally rapid onset and bilateral
- rigidity and rest tremor are uncommon

Unexpl

Diagnosis is usually clinical. However, if there is difficulty differentiating between essential tremor and Parkinson's disease NICE recommend considering ^{123}I -FP-CIT single photon emission computed tomography (SPECT).

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rigidity and rest tremor are uncommon

Diagnosis is usually clinical. However, if there is difficulty differentiating between essential tremor and Parkinson's disease NICE recommend considering ^{123}I -FP-CIT single photon emission computed tomography (SPECT).

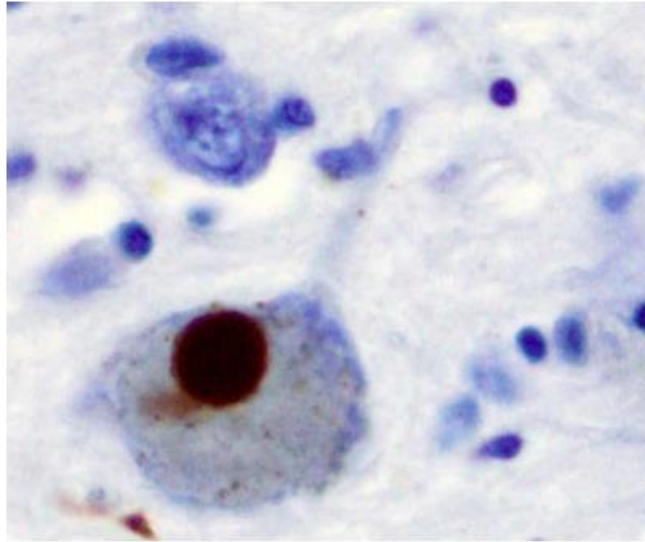


Image sourced from Wikipedia

A Lewy body (stained brown) in a brain cell of the substantia nigra in Parkinson's disease. The brown colour is positive immunohistochemistry staining for alpha-synuclein.



Normal substantia nigra



Loss of pigmented cells in Parkinson's

5 mm

Image sourced from Wikipedia

Discoloration of the substantia nigra due to loss of pigmented nerve cells.

Back to top

Parkinson's disease: management

NICE published guidelines in 2017 regarding the management of Parkinson's disease.

For first-line treatment:

- if the motor symptoms are affecting the patient's quality of life: levodopa
- if the motor symptoms are not affecting the patient's quality of life: dopamine agonist (non-ergot derived), levodopa or monoamine oxidase B (MAO-B) inhibitor

Whilst all drugs used to treat Parkinson's can cause a wide variety of side-effects NICE produced tables to help with decision making:

	Levodopa	Dopamine agonists	MAO-B inhibitors
Motor symptoms	More improvement in motor symptoms	Less improvement in motor symptoms	Less improvement in motor symptoms
Activities of daily living	More improvement in activities of daily living	Less improvement in activities of daily living	Less improvement in activities of daily living
Motor complications	More motor complications	Fewer motor complications	Fewer motor complications
Adverse events	Fewer specified adverse events*	More specified adverse events*	Fewer specified adverse events*

* excessive sleepiness, hallucinations and impulse control disorders

If a patient continues to have symptoms despite optimal levodopa treatment or has developed dyskinesia then NICE recommend the addition of a dopamine agonist, MAO-B inhibitor or catechol-O-methyl transferase (COMT) inhibitor as an adjunct. Again, NICE summarise the main points in terms of decision making:

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Lab Values, Normal Adult: Laboratory... antibiotics classification chart - Googl...

	Dopamine agonists	MAO-B inhibitors	COMT inhibitors	Amantadine
Motor symptoms	Improvement in motor symptoms	Improvement in motor symptoms	Improvement in motor symptoms	No evidence of improvement in motor symptoms
Activities of daily living	Improvement in activities of daily living	Improvement in activities of daily living	Improvement in activities of daily living	No evidence of improvement in activities of daily living
Off time	More off-time reduction	Off-time reduction	Off-time reduction	No studies reporting this outcome
Adverse events	Intermediate risk of adverse events	Fewer adverse events	More adverse events	No studies reporting this outcome
Hallucinations	More risk of hallucinations	Lower risk of hallucinations	Lower risk of hallucinations	No studies reporting this outcome

Specific points regarding Parkinson's medication

NICE reminds us of the risk of acute akinesia or neuroleptic malignant syndrome if medication is not taken/absorbed (for example due to gastroenteritis) and advise against giving patients a 'drug holiday' for the same reason.

Impulse control disorders have become a significant issue in recent years. These can occur with any dopaminergic therapy but are more common with:

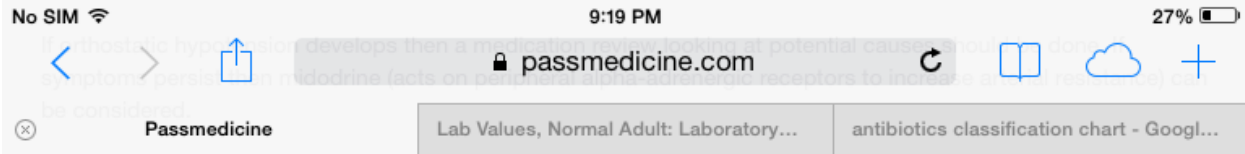
- dopamine agonist therapy
- a history of previous impulsive behaviours
- a history of alcohol consumption and/or smoking

If excessive daytime sleepiness develops then patients should not drive. Medication should be adjusted to control symptoms. Modafinil can be considered if alternative strategies fail.

If orthostatic hypotension develops then a medication review looking at potential causes should be done. If symptoms persist then midodrine (acts on peripheral alpha-adrenergic receptors to increase arterial resistance) can be considered.

Further information regarding specific anti-Parkinson's medication

Levodopa



Further information regarding specific anti-Parkinson's medication

Levodopa

- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis, drowsiness
- no use in neuroleptic induced parkinsonism

Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- more likely than levodopa to cause hallucinations in older patients. Nasal congestion and postural hypotension are also seen in some patients

MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses
- side-effects include ataxia, slurred speech, confusion, dizziness and livedo reticularis

COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone, tolcapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in conjunction with levodopa in patients with established PD

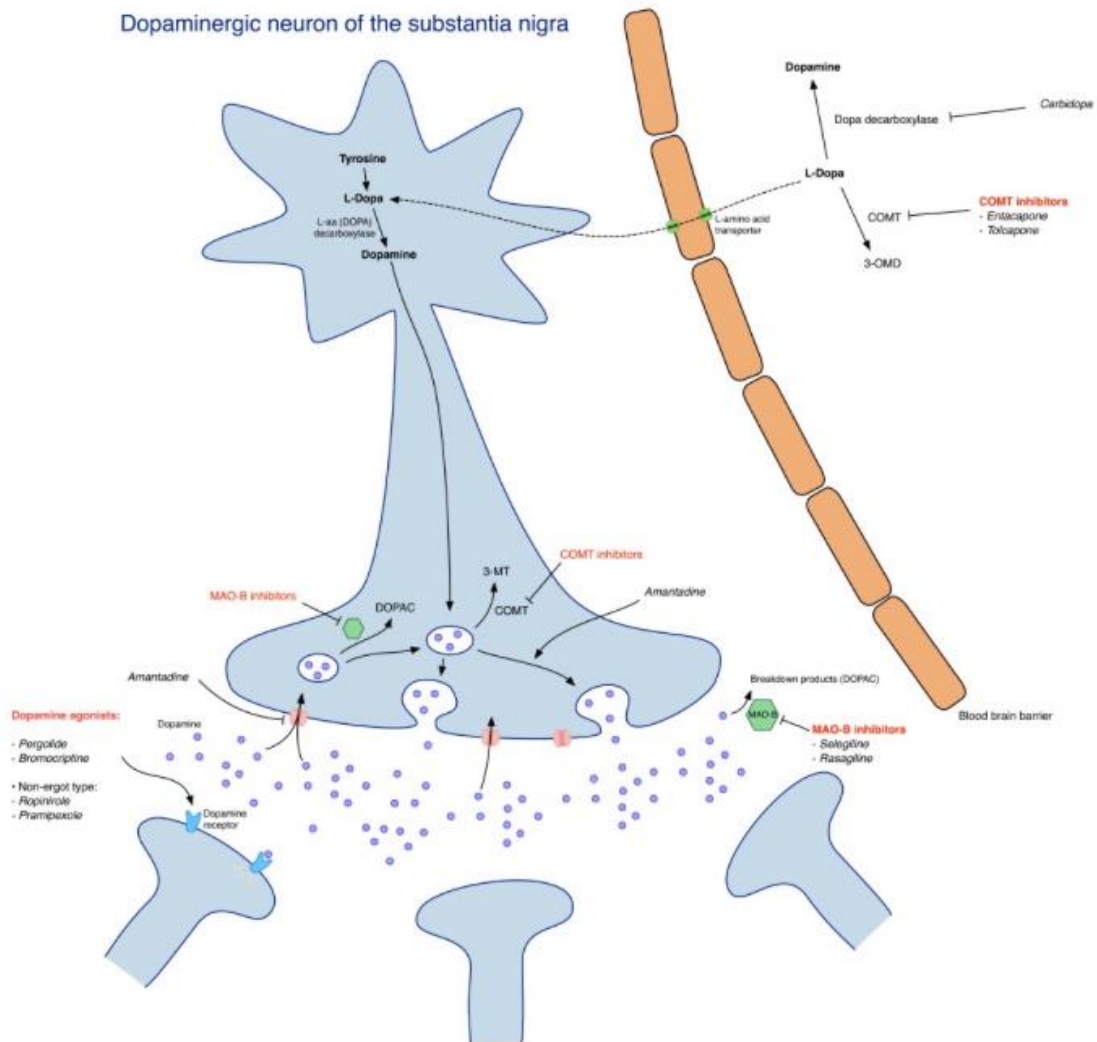
Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. procyclidine, benzotropine, trihexyphenidyl (benzhexol)

COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone, tolcapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in conjunction with levodopa in patients with established PD

Dopaminergic neuron of the substantia nigra



Levodopa

Overview

- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of L-dopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- no use in neuroleptic induced parkinsonism

Adverse effects

- dyskinesia
- 'on-off' effect
- postural hypotension
- cardiac arrhythmias
- nausea & vomiting
- psychosis
- reddish discolouration of urine upon standing

Next question

Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs

Features

- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

Management

- propranolol is first-line
- primidone is sometimes used



Lewy body dementia

Lewy body dementia is an increasingly recognised cause of dementia, accounting for up to 20% of cases. The characteristic pathological feature is alpha-synuclein cytoplasmic inclusions (Lewy bodies) in the substantia nigra, paralimbic and neocortical areas

The relationship between Parkinson's disease and Lewy body dementia is complicated, particularly as dementia is often seen in Parkinson's disease. Also, up to 40% of patients with Alzheimer's have Lewy bodies

Neuroleptics should be avoided in Lewy body dementia as patients are extremely sensitive and may develop irreversible parkinsonism. Questions may give a history of a patient who has deteriorated following the introduction of an antipsychotic agent

Features

- progressive cognitive impairment
- parkinsonism
- visual hallucinations (other features such as delusions and non-visual hallucinations may also be seen)

Diagnosis

- usually clinical
- single-photon emission computed tomography (SPECT) is increasingly used. It is currently commercially known as a DaTscan. Dopaminergic iodine-123-radiolabelled 2-carbomethoxy-3-(4-iodophenyl)-N-(3-fluoropropyl) nortropane (123-I FP-CIT) is used as the radioisotope. The sensitivity of SPECT in diagnosing Lewy body dementia is around 90% with a specificity of 100%

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Normal pressure hydrocephalus

Normal pressure hydrocephalus is a reversible cause of dementia seen in elderly patients. It is thought to be secondary to reduced CSF absorption at the arachnoid villi. These changes may be secondary to head injury, subarachnoid haemorrhage or meningitis.

A classical triad of features is seen

- urinary incontinence
- dementia and bradyphrenia
- gait abnormality (may be similar to Parkinson's disease)

It is thought around 60% of patients will have all 3 features at the time of diagnosis. Symptoms typically develop over a few months.

Imaging

- hydrocephalus with an enlarged fourth ventricle
- in addition to the ventriculomegaly there is typically an absence of substantial sulcal atrophy

Management

- ventriculoperitoneal shunting
- around 10% of patients who have shunts experience significant complications such as seizures, infection and intracerebral haemorrhages

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Head injury: types of traumatic brain injury

Basics

- primary brain injury may be focal (contusion/haematoma) or diffuse (diffuse axonal injury)
- diffuse axonal injury occurs as a result of mechanical shearing following deceleration, causing disruption and tearing of axons
- intra-cranial haematomas can be extradural, subdural or intracerebral, while contusions may occur adjacent to (coup) or contralateral (contre-coup) to the side of impact
- secondary brain injury occurs when cerebral oedema, ischaemia, infection, tonsillar or tentorial herniation exacerbates the original injury. The normal cerebral autoregulatory processes are disrupted following trauma rendering the brain more susceptible to blood flow changes and hypoxia
- the Cushing's reflex (hypertension and bradycardia) often occurs late and is usually a pre terminal event

Type of injury	Notes
Extradural (epidural) haematoma	Bleeding into the space between the dura mater and the skull. Often results from acceleration-deceleration trauma or a blow to the side of the head. The majority of extradural haematomas occur in the temporal region where skull fractures cause a rupture of the middle meningeal artery. Features • features of raised intracranial pressure • some patients may exhibit a lucid interval
Subdural haematoma	Bleeding into the outermost meningeal layer. Most commonly occur around the frontal and parietal lobes. Risk factors include old age, alcoholism and anticoagulation. Slower onset of symptoms than an epidural haematoma.
Subarachnoid haemorrhage	Usually occurs spontaneously in the context of a ruptured cerebral aneurysm but may be seen in association with other injuries when a patient has sustained a traumatic brain injury

Image gallery

Extradural (epidural) haematoma

Next question >

Head injury: NICE guidance on investigation

NICE has strict and clear guidance regarding which adult patients are safe to discharge and which need further CT head imaging. The latter group are also divided into two further cohorts, those who require an immediate CT head and those requiring CT head within 8 hours of injury:

CT head immediately

- GCS < 13 on initial assessment
- GCS < 15 at 2 hours post-injury
- suspected open or depressed skull fracture.
- any sign of basal skull fracture (haemotympanum, 'panda' eyes, cerebrospinal fluid leakage from the ear or nose, Battle's sign).
- post-traumatic seizure.
- focal neurological deficit.
- more than 1 episode of vomiting

CT head scan within 8 hours of the head injury - for adults with any of the following risk factors who have experienced some loss of consciousness or amnesia since the injury:

- age 65 years or older
- any history of bleeding or clotting disorders
- dangerous mechanism of injury (a pedestrian or cyclist struck by a motor vehicle, an occupant ejected from a motor vehicle or a fall from a height of greater than 1 metre or 5 stairs)
- more than 30 minutes' retrograde amnesia of events immediately before the head injury

If a patient is on warfarin who have sustained a head injury with no other indications for a CT head scan, perform a CT head scan within 8 hours of the injury.

Next question >

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Subdural haemorrhage

Basics

- most commonly secondary to trauma e.g. old person/alcohol falling over
- initial injury may be minor and is often forgotten
- caused by bleeding from damaged bridging veins between cortex and venous sinuses

Features

- headache
- classically fluctuating conscious level
- raised ICP

Treatment

- needs neurosurgical review ? burr hole

Next question >

Subarachnoid haemorrhage

Features

- classically: sudden onset severe occipital headache - 'kicked in the back of the head'

Causes

- 85% are due to rupture of berry aneurysms (conditions associated with berry aneurysms include adult polycystic kidney disease, Ehlers-Danlos syndrome and coarctation of the aorta)
- AV malformations
- trauma
- tumours

Investigations

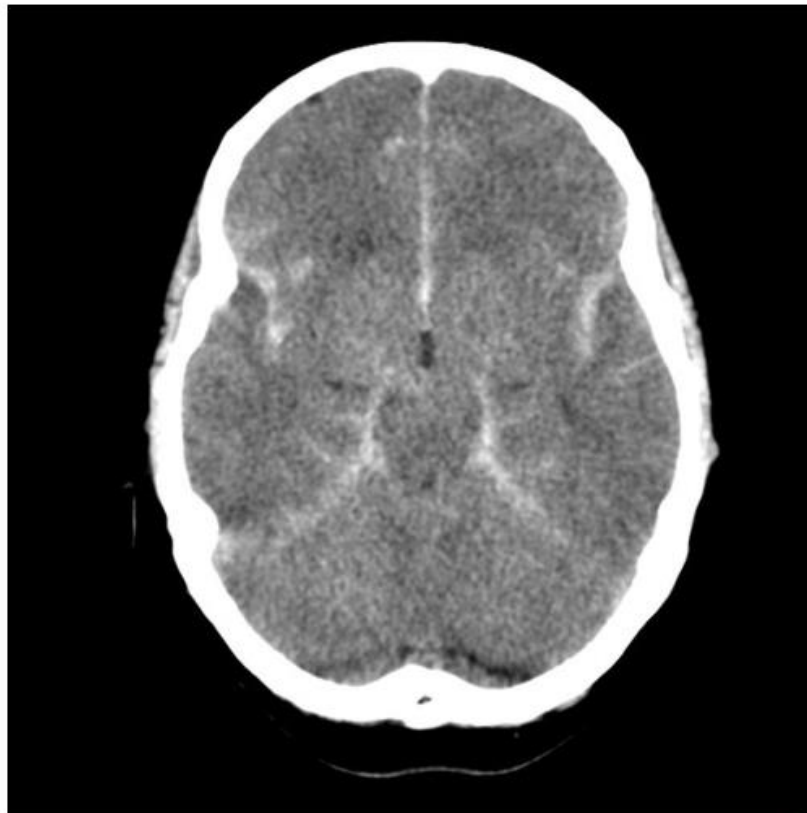
- CT: negative in 5%
- lumbar puncture: done after 12 hrs (allowing time for xanthochromia to develop)

Complications

- rebleeding (in 30%)
- obstructive hydrocephalus (due to blood in ventricles)
- vasospasm leading to cerebral ischaemia

Management

- neurosurgical opinion: no clear evidence over early surgical intervention against delayed intervention
- post-operative nimodipine (e.g. 60mg / 4 hrly, if BP allows) has been shown to reduce the severity of neurological deficits but doesn't reduce rebleeding*

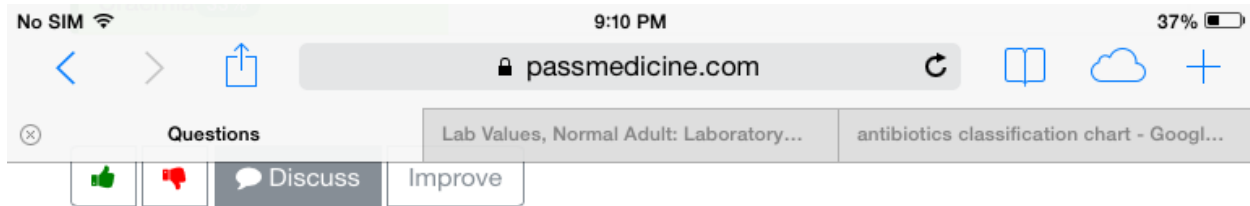


© Image used on license from Radiopaedia

CT image shows diffuse subarachnoid haemorrhage in all basal cisterns, bilateral sylvian fissures and the inter-hemispheric fissure. This case demonstrates the typical distribution that takes the blood into the subarachnoid space in a subarachnoid hemorrhage.

*the way nimodipine works in subarachnoid haemorrhage is not fully understood. It has been previously postulated that it reduces cerebral vasospasm (hence maintaining cerebral perfusion) but this has not been demonstrated in studies





Next question >

Peripheral neuropathy

Peripheral neuropathy may be divided into conditions which predominately cause a motor or sensory loss

Predominately motor loss

- Guillain-Barre syndrome
- porphyria
- lead poisoning
- hereditary sensorimotor neuropathies (HSMN) - Charcot-Marie-Tooth
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- diphtheria

Predominately sensory loss

- diabetes
- uraemia
- leprosy
- alcoholism
- vitamin B12 deficiency
- amyloidosis

Alcoholic neuropathy

- secondary to both direct toxic effects and reduced absorption of B vitamins
- sensory symptoms typically present prior to motor symptoms

Vitamin B12 deficiency

- subacute combined degeneration of spinal cord
- dorsal column usually affected first (joint position, vibration) prior to distal paraesthesia

Next question >

Drugs causing peripheral neuropathy

Drugs causing a peripheral neuropathy

- amiodarone
- isoniazid
- vincristine
- nitrofurantoin
- metronidazole

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Score for this session: 50%

2 in a row correct

Key facts from this session are shown below (score/attempts), click on the fact for background information

Metronidazole may cause peripheral neuropathy

[Notes](#) (1/1)

A woman suddenly falls to the ground then lays motionless - atonic seizures

[Notes](#) (1/1)

Carbamazepine may cause diplopia

[Notes](#) (0/1)

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*if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

Ataxic telangiectasia

Ataxic telangiectasia is an autosomal recessive disorder caused by a defect in the ATM gene which encodes for DNA repair enzymes. It is one of the inherited combined immunodeficiency disorders. It typically presents in early childhood with abnormal movements.

Features

- cerebellar ataxia
- telangiectasia (spider angiomas)
- IgA deficiency resulting in recurrent chest infections
- 10% risk of developing malignancy, lymphoma or leukaemia, but also non-lymphoid tumours

Friedreich's ataxia

Friedreich's ataxia is the most common of the early-onset hereditary ataxias. It is an autosomal recessive, trinucleotide repeat disorder characterised by a GAA repeat in the X25 gene on chromosome 9 (frataxin). Friedreich's ataxia is unusual amongst trinucleotide repeat disorders in not demonstrating the phenomenon of anticipation.

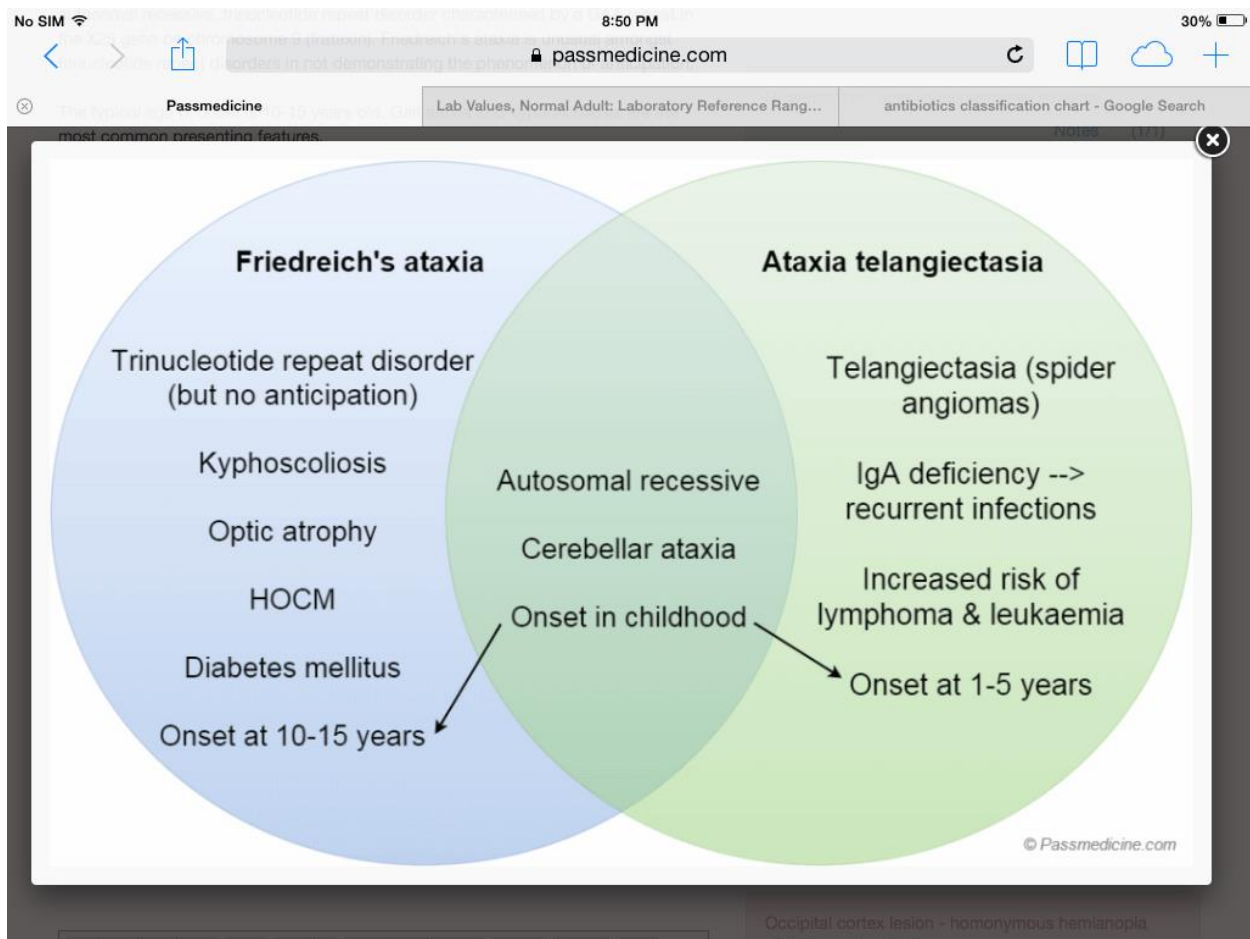
The typical age of onset is 10-15 years old. Gait ataxia and kyphoscoliosis are the most common presenting features.

Neurological features

- absent ankle jerks/extensor plantars
- cerebellar ataxia
- optic atrophy
- spinocerebellar tract degeneration

Other features

- hypertrophic obstructive cardiomyopathy (90%, most common cause of death)
- diabetes mellitus (10-20%)
- high-arched palate



Hemiballism

Hemiballism occurs following damage to the subthalamic nucleus. Ballistic movements are involuntary, sudden, jerking movements which occur contralateral to the side of the lesion. The ballistic movements primarily affect the proximal limb musculature whilst the distal muscles may display more choreiform-like movements

Symptoms may decrease whilst the patient is asleep.

Antidopaminergic agents (e.g. Haloperidol) are the mainstay of treatment

Next question >

Chorea

Chorea describes involuntary, rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus.

Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- pregnancy: chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

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Reference rangesEnd session

Question

Which one of the following is a cause of chorea?

Proximodistal

Flushing

Parkinsonism

Hypotension

Tardive dyskinesia

Hyperreflexia

Huntington's disease

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Huntington's disease is an inherited neurodegenerative condition. It is a progressive and incurable condition that typically results in death 20 years after the initial symptoms develop.

Genetics

- autosomal dominant
- trinucleotide repeat disorder: repeat expansion of CAG
- results in degeneration of cholinergic and GABAergic neurons in the striatum of the basal ganglia
- due to defect in huntingtin gene on chromosome 4

Features typical develop after 35 years of age

- chorea
- personality changes (e.g. irritability, apathy, depression) and intellectual impairment
- dystonia
- saccadic eye movements

Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleeps (PLMS)

Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

Management

- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

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Macroglossia

Causes

- hypothyroidism
- acromegaly
- amyloidosis
- Duchenne muscular dystrophy
- mucopolysaccharidosis (e.g. Hurler syndrome)

Patients with Down's syndrome are now thought to have apparent macroglossia due to a combination of mid-face hypoplasia and hypotonia

Next question >

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Myasthenia gravis

Myasthenia gravis is an autoimmune disorder resulting in insufficient functioning acetylcholine receptors. Antibodies to acetylcholine receptors are seen in 85-90% of cases*. Myasthenia is more common in women (2:1)

The key feature is muscle fatigability - muscles become progressively weaker during periods of activity and slowly improve after periods of rest:

- extraocular muscle weakness: diplopia
- proximal muscle weakness: face, neck, limb girdle
- ptosis
- dysphagia

Associations

- thymomas in 15%
- autoimmune disorders: pernicious anaemia, autoimmune thyroid disorders, rheumatoid, SLE
- thymic hyperplasia in 50-70%

Investigations

- single fibre electromyography: high sensitivity (92-100%)
- CT thorax to exclude thymoma
- CK normal
- autoantibodies: around 85-90% of patients have antibodies to acetylcholine receptors. In the remaining patients, about 40% are positive for anti-muscle-specific tyrosine kinase antibodies
- Tensilon test: IV edrophonium reduces muscle weakness temporarily - not commonly used anymore due to the risk of cardiac arrhythmia

Management

- long-acting anticholinesterase e.g. pyridostigmine
- immunosuppression: prednisolone initially
- thymectomy

Management of myasthenic crisis

- plasmapheresis
- intravenous immunoglobulins

*antibodies are less commonly seen in disease limited to the ocular muscles

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Amoxicillin is generally considered to be safe in myasthenia gravis.



Next question >

Myasthenia gravis: exacerbating factors

The most common exacerbating factor is exertion resulting in fatigability, which is the hallmark feature of myasthenia gravis . Symptoms become more marked during the day

The following drugs may exacerbate myasthenia:

- penicillamine
- quinidine, procainamide
- beta-blockers
- lithium
- phenytoin
- antibiotics: gentamicin, macrolides, quinolones, tetracyclines

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HSMN

Hereditary sensorimotor neuropathy (HSMN) is a relatively new term which encompasses Charcot-Marie-Tooth disease (also known as peroneal muscular atrophy). Over 7 types have been characterised - however only 2 are common to clinical practice

- HSMN type I: primarily due to demyelinating pathology
- HSMN type II: primarily due to axonal pathology

HSMN type I

- autosomal dominant
- due to defect in PMP-22 gene (which codes for myelin)
- features often start at puberty
- motor symptoms predominate
- distal muscle wasting, pes cavus, clawed toes
- foot drop, leg weakness often first features



CADASIL

Overview

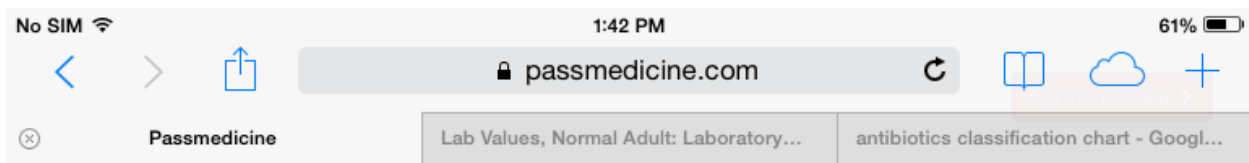
- Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL)
- rare cause of multi-infarct dementia
- patients often present with migraine

Next question >

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Creutzfeldt-Jakob disease

Creutzfeldt-Jakob disease (CJD) is rapidly progressive neurological condition caused by prion proteins. These proteins induce the formation of amyloid folds resulting in tightly packed beta-pleated sheets resistant to proteases.

Features

- dementia (rapid onset)
- myoclonus

Investigation

- CSF is usually normal
- EEG: biphasic, high amplitude sharp waves (only in sporadic CJD)
- MRI: hyperintense signals in the basal ganglia and thalamus

Sporadic CJD

- accounts for 85% of cases
- 10-15% of cases are familial
- mean age of onset is 65 years

New variant CJD

- younger patients (average age of onset = 25 years)
- psychological symptoms such as anxiety, withdrawal and dysphonia are the most common presenting features
- the 'prion protein' is encoded on chromosome 20 - it's role is not yet understood
- methionine homozygosity at codon 129 of the prion protein is a risk factor for developing CJD - all patients who have so far died have had this
- median survival = 13 months

Other prion diseases

- kuru
- fatal familial insomnia
- Gerstmann Straussler-Scheinker disease

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Questions

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Brain MRI not meeting criteria for MS at disease onset

Spinal MRI with contiguous T2-weighted signal abnormality extending over three or more vertebral segments

NMO-IgG seropositive status (The NMO-IgG test checks the existence of antibodies against the aquaporin 4 antigen.)

Compared to multiple sclerosis, the acute episodes are not understood to be triggered by the immune system's T cells, but rather by antibodies called NMO-IgG.



 Discuss
  Improve

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Neuromyelitis optica

Neuromyelitis optica (NMO) is monophasic or relapsing-remitting demyelinating CNS disorder. Although previously thought to be a variant of multiple sclerosis, it is now recognised to be a distinct disease, particularly prevalent in Asian populations¹. It typically involves the optic nerves and cervical spine, with imaging of the brain frequently normal. Vomiting is also a common presenting complaint.

Diagnosis requires bilateral optic neuritis, myelitis and 2 of the follow 3 criteria²:

- 1. Spinal cord lesion involving 3 or more spinal levels
- 2. Initially normal MRI brain
- 3. Aquaporin 4 positive serum antibody

1. Wingerchuk DM, Lennon VA, Lucchinetti CF et al. The spectrum of neuromyelitis optica. *Lancet Neurol*. 2007;6(9):805.

2. Wingerchuk DM, Lennon VA, Pittock SJ et al. Revised diagnostic criteria for neuromyelitis optica. *Neurology*. 2006;66(10):1485.

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Multiple sclerosis: features

Patient's with multiple sclerosis (MS) may present with non-specific features, for example around 75% of patients have significant lethargy.

Visual

- optic neuritis: common presenting feature
- optic atrophy
- Uhthoff's phenomenon: worsening of vision following rise in body temperature
- internuclear ophthalmoplegia

Sensory

- pins/needles
- numbness
- trigeminal neuralgia
- Lhermitte's syndrome: paraesthesiae in limbs on neck flexion

Motor

- spastic weakness: most commonly seen in the legs

Cerebellar

- ataxia: more often seen during an acute relapse than as a presenting symptom
- tremor

Others

- urinary incontinence
- sexual dysfunction
- intellectual deterioration

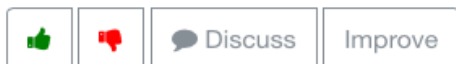
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NICE

[2014 Multiple sclerosis guidelines](#)

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Next question >

Multiple sclerosis: prognostic features

Good prognosis features

- female sex
- young age of onset (i.e. 20s or 30s)
- relapsing-remitting disease
- sensory symptoms only
- long interval between first two relapses
- complete recovery between relapses

Ways of remembering prognostic features

- the typical patient carries a better prognosis than an atypical presentation

Next question >

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Multiple sclerosis: investigation

Diagnosis requires demonstration of lesions disseminated in time and space

MRI

- high signal T2 lesions
- periventricular plaques
- Dawson fingers: often seen on FLAIR images - hyperintense lesions penpendicular to the corpus callosum

CSF

- oligoclonal bands (and not in serum)
- increased intrathecal synthesis of IgG

Visual evoked potentials

- delayed, but well preserved waveform

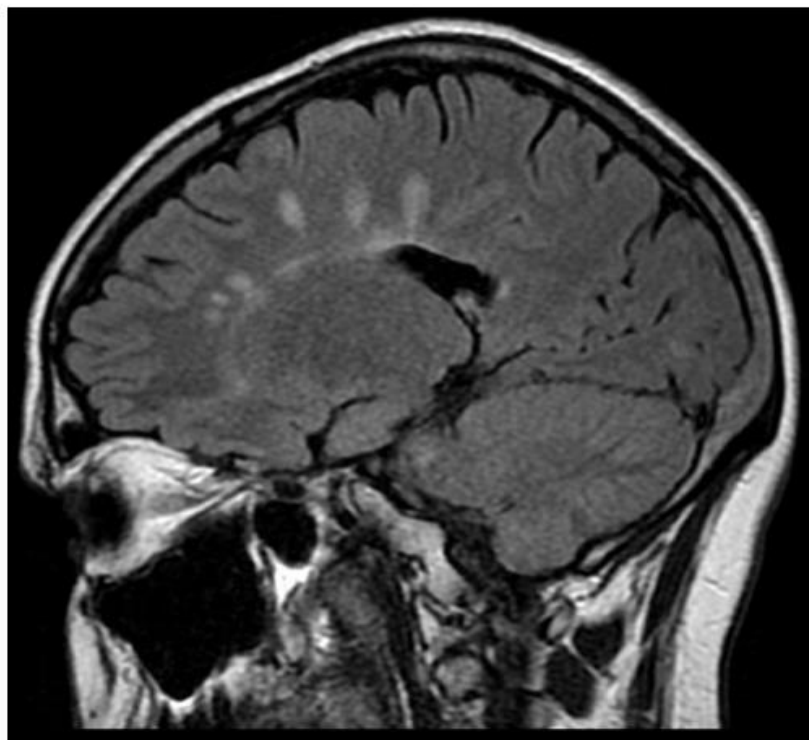


Image used on license from Radiopaedia

MRI showing multiple white matter plaques penpendicular to the corpus callosum giving the appearance of Dawson fingers

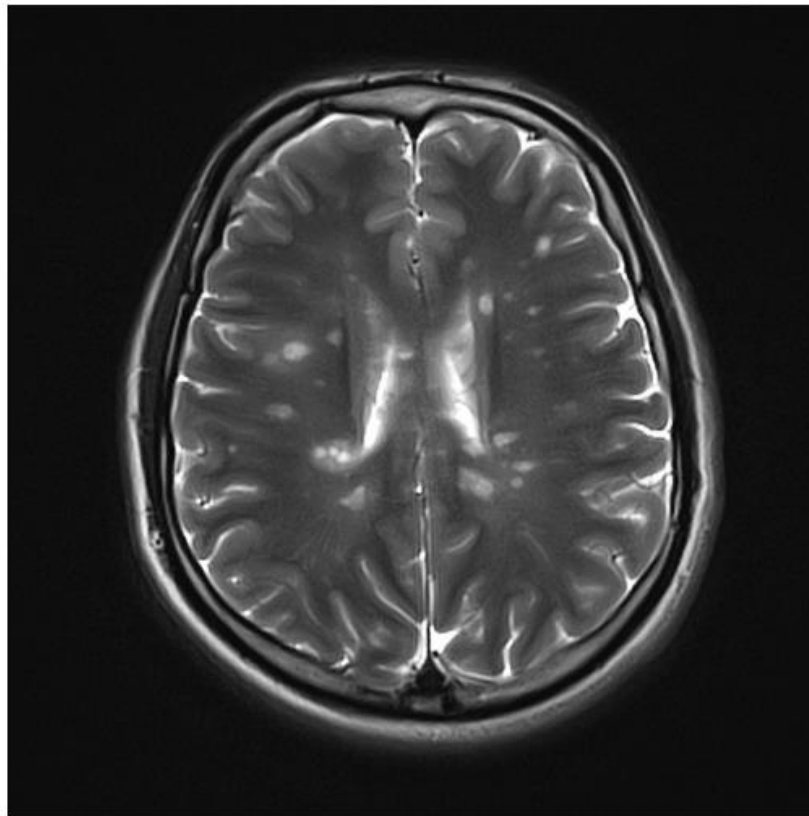
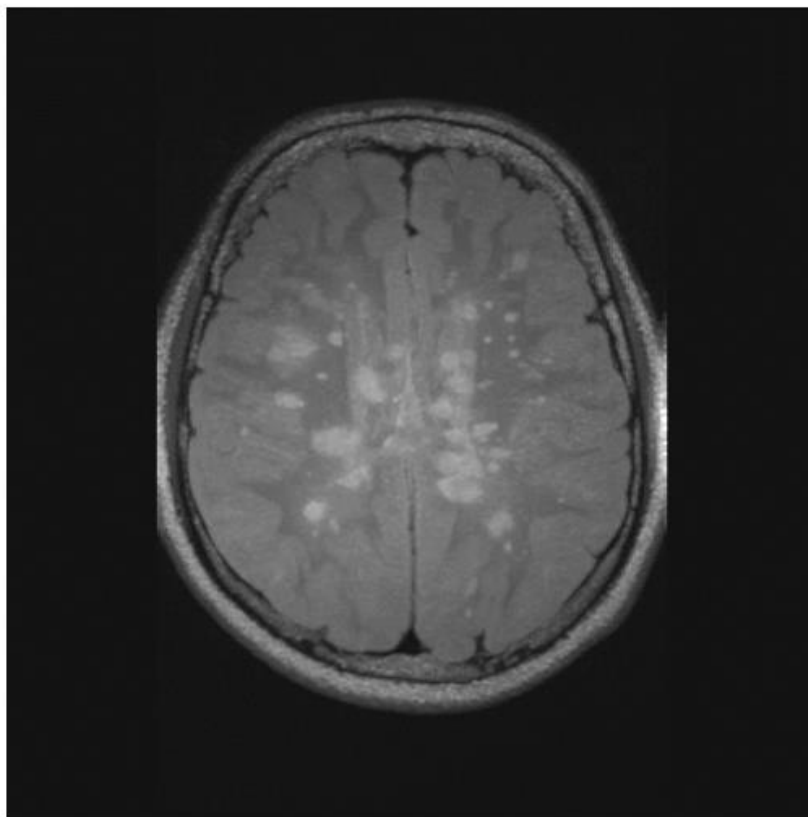


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MRI from a young patient with multiple sclerosis. Widespread periventricular, juxtacortical, post fossa and upper cervical cord high T2 regions are noted. Note the difference in the lesions with varying degrees of contrast enhancement and restricted diffusion indicating active/recent demyelination. This satisfies the diagnostic criteria in terms of separation in terms of time space.

terms of time space.



© Image used on license from Radiopaedia

MRI FLAIR from the same patient as above. The numerous lesions are more easily identified than in the above T2 image.

Next question >

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Reduced wave amplitude 16%

Slowing of the nerve conduction velocity usually indicates there is damage to the myelin sheath, as in Guillain-Barre syndrome



Next question >

Nerve conduction studies

Nerve conduction studies (NCS) are useful in determining between axonal and demyelinating pathology

Axonal

- normal conduction velocity
- reduced amplitude

Demyelinating

- reduced conduction velocity
- normal amplitude

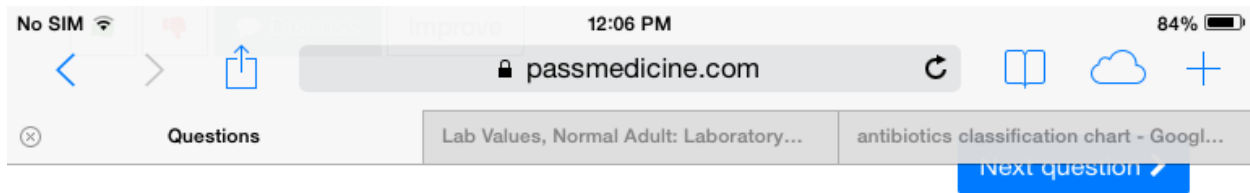
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Multiple sclerosis: management

Treatment in multiple sclerosis is focused at reducing the frequency and duration of relapses. There is no cure.

Acute relapse

High dose steroids (e.g. oral or IV methylprednisolone) may be given for 5 days to shorten the length of an acute relapse. It should be noted that steroids shorten the duration of a relapse and do not alter the degree of recovery (i.e. whether a patient returns to baseline function)

Disease modifying drugs

Beta-interferon has been shown to reduce the relapse rate by up to 30%. Certain criteria have to be met before it is used:

- relapsing-remitting disease + 2 relapses in past 2 years + able to walk 100m unaided
- secondary progressive disease + 2 relapses in past 2 years + able to walk 10m (aided or unaided)
- reduces number of relapses and MRI changes, however doesn't reduce overall disability

Other drugs used in the management of multiple sclerosis include:

- glatiramer acetate: immunomodulating drug - acts as an 'immune decoy'
- natalizumab: a recombinant monoclonal antibody that antagonises Alpha-4 Beta-1-integrin found on the surface of leucocytes, thus inhibiting migration of leucocytes across the endothelium across the blood-brain barrier
- fingolimod: sphingosine 1-phosphate receptor modulator, prevents lymphocytes from leaving lymph nodes. An oral formulation is available

Some specific problems

Fatigue

- once other problems (e.g. anaemia, thyroid or depression) have been excluded NICE recommend a trial of amantadine
- other options include mindfulness training and CBT

Spasticity

- baclofen and gabapentin are first-line. Other options include diazepam, dantrolene and tizanidine
- physiotherapy is important
- cannabis and botox are undergoing evaluation

Bladder dysfunction

- may take the form of urgency, incontinence, overflow etc
- guidelines stress the importance of getting an ultrasound first to assess bladder emptying
 - anticholinergics may worsen symptoms in some patients
- if significant residual volume → intermittent self-catheterisation
- if no significant residual volume → anticholinergics may improve urinary frequency

Oscillopsia (visual fields appear to oscillate)

- gabapentin is first-line

Next question >

No SIM 3:16 PM 69%

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Questions

Lab Values, Normal Adult: Laboratory... antibiotics classification chart - Googl...

HIV 13%



 Discuss (2) Improve

Next question >

Autonomic neuropathy

Features

- impotence, inability to sweat, postural hypotension
- postural hypotension e.g. drop of 30/15 mmHg
- loss of decrease in heart rate following deep breathing
- pupils: dilates following adrenaline instillation

Causes

- diabetes
- Guillain-Barre syndrome
- multisystem atrophy (MSA), Shy-Drager syndrome
- Parkinson's
- infections: HIV, Chagas' disease, neurosyphilis
- drugs: antihypertensives, tricyclics
- craniopharyngioma

Next question >

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Next question >

Rinne's and Weber's test

Performing both Rinne's and Weber's test allows differentiation of conductive and sensorineural deafness.

Rinne's test

- tuning fork is placed over the mastoid process until the sound is no longer heard, followed by repositioning just over external acoustic meatus
- air conduction (AC) is normally better than bone conduction (BC)
- if $BC > AC$ then conductive deafness

Weber's test

- tuning fork is placed in the middle of the forehead equidistant from the patient's ears
- the patient is then asked which side is loudest
- in unilateral sensorineural deafness, sound is localised to the unaffected side
- in unilateral conductive deafness, sound is localised to the affected side

Next question >

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Reference ranges End session

Vertigo

Vertigo may be defined as the false sensation that the body or environment is moving.

The table below lists the main characteristics of the most important causes of vertigo

Disorder	Notes
Viral labyrinthitis	Recent viral infection Sudden onset Nausea and vomiting Hearing may be affected
Vestibular neuronitis	Recent viral infection Recurrent vertigo attacks lasting hours or days No hearing loss
Benign paroxysmal positional vertigo	Gradual onset Triggered by change in head position Each episode lasts 10-20 seconds
Meniere's disease	Associated with hearing loss, tinnitus and sensation of fullness or pressure in one or both ears
Vertebrobasilar ischaemia	Elderly patient Dizziness on extension of neck
Acoustic neuroma	Hearing loss, vertigo, tinnitus Absent corneal reflex is important sign Associated with neurofibromatosis type 2

Other causes of vertigo include

- trauma
- multiple sclerosis
- ototoxicity e.g. gentamicin

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Benign paroxysmal positional vertigo

Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of vertigo encountered. It is characterised by the sudden onset of dizziness and vertigo triggered by changes in head position. The average age of onset is 55 years and it is less common in younger patients.

Features

- vertigo triggered by change in head position (e.g. rolling over in bed or gazing upwards)
- may be associated with nausea
- each episode typically lasts 10-20 seconds
- positive Dix-Hallpike manoeuvre

BPPV has a good prognosis and usually resolves spontaneously after a few weeks to months. Symptomatic relief may be gained by:

- **Epley manoeuvre** (successful in around 80% of cases)
- teaching the patient exercises they can do themselves at home, termed vestibular rehabilitation, for example Brandt-Daroff exercises

Medication is often prescribed (e.g. Betahistine) but it tends to be of limited value.

Acoustic neuroma

Acoustic neuromas (more correctly called vestibular schwannomas) account for approximately five percent of intracranial tumours and 90 percent of cerebellopontine angle

Features can be predicted by the affected cranial nerves

- cranial nerve VIII: hearing loss, vertigo, tinnitus
- cranial nerve V: absent corneal reflex
- cranial nerve VII: facial palsy

Bilateral acoustic neuromas are seen in neurofibromatosis type 2

MRI of the cerebellopontine angle is the investigation of choice

Meniere's disease

Meniere's disease is a disorder of the inner ear of unknown cause. It is characterised by excessive pressure and progressive dilation of the endolymphatic system. It is more common in middle-aged adults but may be seen at any age. Meniere's disease has a similar prevalence in both men and women.

Features

- recurrent episodes of vertigo, tinnitus and hearing loss (sensorineural). Vertigo is usually the prominent symptom
- a sensation of aural fullness or pressure is now recognised as being common
- other features include nystagmus and a positive Romberg test
- episodes last minutes to hours
- typically symptoms are unilateral but bilateral symptoms may develop after a number of years

Natural history

- symptoms resolve in the majority of patients after 5-10 years
- the majority of patients will be left with a degree of hearing loss
- psychological distress is common

Management

- ENT assessment is required to confirm the diagnosis
- patients should inform the DVLA. The current advice is to cease driving until satisfactory control of symptoms is achieved
- acute attacks: buccal or intramuscular prochlorperazine. Admission is sometimes required
- prevention: betahistine and vestibular rehabilitation exercises may be of benefit

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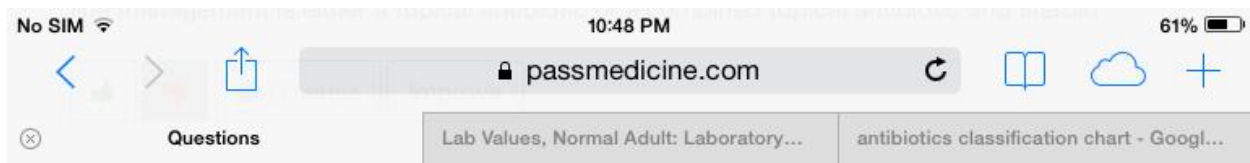
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Clinical Knowledge Summaries

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[Meniere's disease guidelines](#)

(1/1)



Otitis externa

Otitis externa is a common reason for primary care attendance in the UK.

Causes of otitis externa include:

- infection: bacterial (*Staphylococcus aureus*, *Pseudomonas aeruginosa*) or fungal
- seborrhoeic dermatitis
- contact dermatitis (allergic and irritant)

Features

- ear pain, itch, discharge
- otoscopy: red, swollen, or eczematous canal

The recommend initial management of otitis externa is:

- topical antibiotic or a combined topical antibiotic with steroid
- if the tympanic membrane is perforated aminoglycosides are traditionally not used*
- if there is canal debris then consider removal
- if the canal is extensively swollen then an ear wick is sometimes inserted

Second line options include

- consider contact dermatitis secondary to neomycin
- oral antibiotics if the infection is spreading
- taking a swab inside the ear canal
- empirical use of an antifungal agent

Malignant otitis externa is more common in elderly diabetics. In this condition there is extension of infection into the bony ear canal and the soft tissues deep to the bony canal. Intravenous antibiotics may be required.

*many ENT doctors disagree with this and feel that concerns about ototoxicity are unfounded

Next question >

Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details.

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Brain lesions

The following neurological disorders/features may allow localisation of a brain lesion:

Gross anatomy

Parietal lobe lesions

- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

Occipital lobe lesions

- homonymous hemianopia (with macula sparing)
- cortical blindness
- visual agnosia

Temporal lobe lesion

- Wernicke's aphasia: this area 'forms' the speech before 'sending it' to Broca's area. Lesions result in word substitution, neologisms but speech remains fluent
- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

Frontal lobes lesions

- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus. Speech is non-fluent, laboured, and halting
- disinhibition
- perseveration
- anosmia
- inability to generate a list

Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysidiadokinesis, nystagmus

More specific areas

Area	Associated conditions
Medial temporal lobe and hippocampus: lesion of the hippocampus	Amnesia and Korsakoff's syndrome

Stroke: types

The **Oxford Stroke Classification** (also known as the Bamford Classification) classifies strokes based on the initial symptoms. A summary is as follows:

The following criteria should be assessed:

- 1. unilateral hemiparesis and/or hemisensory loss of the face, arm & leg
- 2. homonymous hemianopia
- 3. higher cognitive dysfunction e.g. dysphasia

Total anterior circulation infarcts (TACI, c. 15%)

- involves middle and anterior cerebral arteries
- all 3 of the above criteria are present

Partial anterior circulation infarcts (PACI, c. 25%)

- involves smaller arteries of anterior circulation e.g. upper or lower division of middle cerebral artery
- 2 of the above criteria are present

Lacunar infarcts (LACI, c. 25%)

- involves perforating arteries around the internal capsule, thalamus and basal ganglia
- presents with 1 of the following:
 - 1. unilateral weakness (and/or sensory deficit) of face and arm, arm and leg or all three.
 - 2. pure sensory stroke.
 - 3. ataxic hemiparesis

Posterior circulation infarcts (POCI, c. 25%)

- involves vertebrobasilar arteries
- presents with 1 of the following:
 - 1. cerebellar or brainstem syndromes
 - 2. loss of consciousness
 - 3. isolated homonymous hemianopia

Other recognised patterns of stroke:

Other recognised patterns of stroke:

Lateral medullary syndrome (posterior inferior cerebellar artery)

- aka Wallenberg's syndrome
- ipsilateral: ataxia, nystagmus, dysphagia, facial numbness, cranial nerve palsy e.g. Horner's
- contralateral: limb sensory loss

Weber's syndrome

- ipsilateral III palsy
- contralateral weakness

Medulla

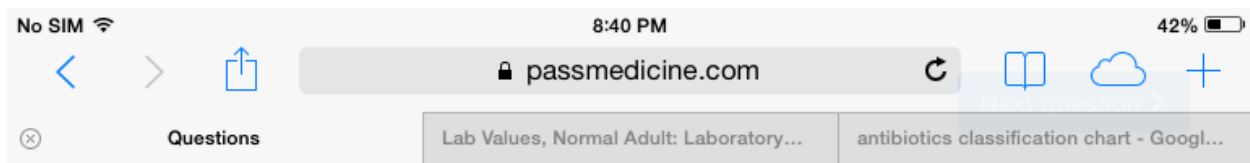
Stroke by anatomy

Site of the lesion	Associated effects
Anterior cerebral artery	Contralateral hemiparesis and sensory loss, lower extremity > upper
Middle cerebral artery	Contralateral hemiparesis and sensory loss, upper extremity > lower Contralateral homonymous hemianopia Aphasia
Posterior cerebral artery	Contralateral homonymous hemianopia with macular sparing Visual agnosia
Weber's syndrome (branches of the posterior cerebral artery that supply the midbrain)	Ipsilateral CN III palsy Contralateral weakness of upper and lower extremity
Posterior inferior cerebellar artery (lateral medullary syndrome, Wallenberg syndrome)	Ipsilateral: facial pain and temperature loss Contralateral: limb/torso pain and temperature loss Ataxia, nystagmus
Anterior inferior cerebellar artery (lateral pontine syndrome)	Symptoms are similar to Wallenberg's (see above), but: Ipsilateral: facial paralysis and deafness
Retinal/ophthalmic artery	Amaurosis fugax
Basilar artery	'Locked-in' syndrome

Lacunar strokes

- present with either isolated hemiparesis, hemisensory loss or hemiparesis with limb ataxia
- strong association with hypertension
- common sites include the basal ganglia, thalamus and internal capsule

B I U T!



Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued stroke guidelines in 2008, although they modified their guidance with respect to antiplatelet therapy in 2010.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy*
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commenced on a statin. Many physicians will delay treatment until after at least 48 hours due to the risk of haemorrhagic transformation

Thrombolysis

Thrombolysis should only be given if:

- it is administered within 4.5 hours of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE.

Contraindications to thrombolysis:

Absolute	Relative
- Previous intracranial haemorrhage - Seizure at onset of stroke - Intracranial neoplasm	- Concurrent anticoagulation (INR > 1.7) - Haemorrhagic diathesis - Active diabetic haemorrhagic

Absolute	Relative
- Previous intracranial haemorrhage - Seizure at onset of stroke - Intracranial neoplasm - Suspected subarachnoid haemorrhage - Stroke or traumatic brain injury in preceding 3 months - Lumbar puncture in preceding 7 days - Gastrointestinal haemorrhage in preceding 3 weeks - Active bleeding - Pregnancy - Oesophageal varices - Uncontrolled hypertension >200/120mmHg	- Concurrent anticoagulation (INR >1.7) - Haemorrhagic diathesis - Active diabetic haemorrhagic retinopathy - Suspected intracardiac thrombus - Major surgery / trauma in preceding 2 weeks

Secondary prevention

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- clopidogrel is now recommended by NICE ahead of combination use of aspirin plus modified release (MR) dipyridamole in people who have had an ischaemic stroke
- aspirin plus MR dipyridamole is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to 2 years' duration
- MR dipyridamole alone is recommended after an ischaemic stroke only if aspirin or clopidogrel are contraindicated or not tolerated, again with no limit on duration of treatment

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST** criteria or > 50% according to NASCET*** criteria

*the 2009 Controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial may change thinking on this but guidelines have yet to change to reflect this

**European Carotid Surgery Trialists' Collaborative Group

***North American Symptomatic Carotid Endarterectomy Trial

Next question >

No SIM 2:27 PM 75%

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Questions

Lab Values, Normal Adult: Laboratory...

antibiotics classification chart - Googl...

Multiple sclerosis	22%
Parasagittal meningioma	17%

Amyloidosis is the least likely of the above options to result in a spastic paraparesis



[Discuss \(1\)](#)
[Improve](#)

[Next question >](#)

Spastic paraparesis

Spastic paraparesis describes a upper motor neuron pattern of weakness in the lower limbs

Causes

- demyelination e.g. multiple sclerosis
- cord compression: trauma, tumour
- parasagittal meningioma
- tropical spastic paraparesis
- transverse myelitis e.g. HIV
- syringomyelia
- hereditary spastic paraplegia
- osteoarthritis of the cervical spine

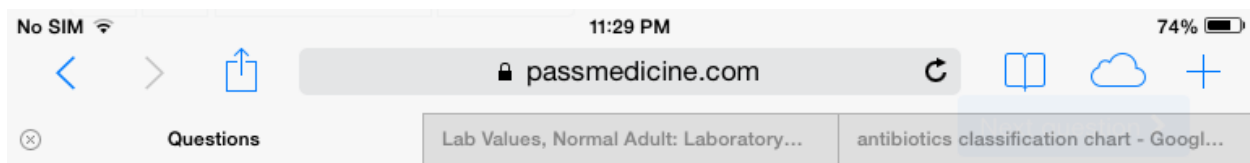
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Transient ischaemic attack

Assessment and referral

The ABCD2 prognostic score has previously been used to risk stratify patients who present with a suspected TIA. However, data from studies have suggested it performs poorly and it is therefore no longer recommended by NICE Clinical Knowledge Summaries. Instead, NICE recommend:

Immediate antithrombotic therapy:

- give aspirin 300 mg immediately, unless
- 1. the patient has a bleeding disorder or is taking an anticoagulant (needs immediate admission for imaging to exclude a haemorrhage)
- 2. the patient is already taking low-dose aspirin regularly: continue the current dose of aspirin until reviewed by a specialist
- 3. Aspirin is contraindicated: discuss management urgently with the specialist team

If the patient has had more than 1 TIA ('crescendo TIA') or has a suspected cardioembolic source or severe carotid stenosis:

- discuss the need for admission or observation urgently with a stroke specialist

If the patient has had a suspected TIA in the last 7 days:

- arrange urgent assessment (within 24 hours) by a specialist stroke physician

If the patient has had a suspected TIA which occurred more than a week previously:

- refer for specialist assessment as soon as possible within 7 days

Advise the person not to drive until they have been seen by a specialist.

Further management

Antithrombotic therapy

- clopidogrel is recommended first-line (as for patients who've had a stroke)
- aspirin + dipyridamole should be given to patients who cannot tolerate clopidogrel
- these recommendations follow the 2012 Royal College of Physicians National clinical guideline for stroke. Please see the link for more details (section 5.5)
- these guidelines may change following the CHANCE study (NEJM 2013;369:11). This study looked at giving high-risk TIA patients aspirin + clopidogrel for the first 90 days compared to aspirin alone. 11.7% of aspirin only patients had a stroke over 90 days compared to 8.2% of dual antiplatelet patients

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST* criteria or > 50% according to NASCET** criteria

*European Carotid Surgery Trialists' Collaborative Group

**North American Symptomatic Carotid Endarterectomy Trial

Next question >



Intracranial venous thrombosis



Overview

- can cause cerebral infarction, much less common than arterial causes
- 50% of patients have isolated sagittal sinus thromboses - the remainder have coexistent lateral sinus thromboses and cavernous sinus thromboses

Features

- headache (may be sudden onset)
- nausea & vomiting

Sagittal sinus thrombosis

- may present with seizures and hemiplegia
- parasagittal biparietal or bifrontal haemorrhagic infarctions are sometimes seen

Cavernous sinus thrombosis

- other causes of cavernous sinus syndrome: local infection (e.g. sinusitis), neoplasia, trauma
- periorbital oedema
- ophthalmoplegia: 6th nerve damage typically occurs before 3rd & 4th
- trigeminal nerve involvement may lead to hyperaesthesia of upper face and eye pain
- central retinal vein thrombosis

Lateral sinus thrombosis

- 6th and 7th cranial nerve palsies



Slurring of speech 15%

Progressive supranuclear palsy: parkinsonism, impairment of vertical gaze

Impairment of vertical gaze is seen in progressive supranuclear palsy. Horizontal gaze impairment is sometimes seen later as the disease progresses, but would be atypical in a newly diagnosed patient.



Next question >

Progressive supranuclear palsy

Overview

- aka Steele-Richardson-Olszewski syndrome
- a 'Parkinson Plus' syndrome

Features

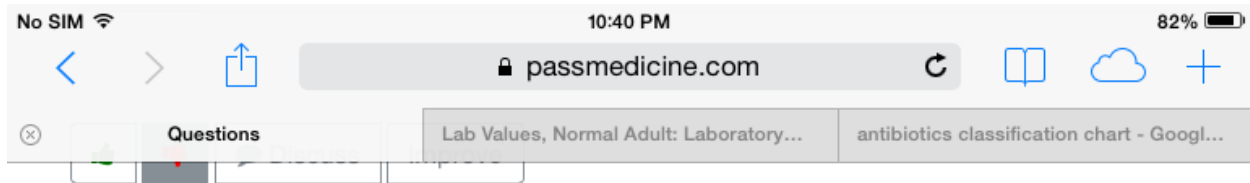
- impairment of vertical gaze (down gaze worse than up gaze - patients may complain of difficulty reading or descending stairs)
- parkinsonism
- falls
- slurring of speech
- cognitive impairment

Management

- poor response to L-dopa

Next question >





Next question >

Complex regional pain syndrome

Complex regional pain syndrome (CRPS) is the modern, umbrella term for a number of conditions such as reflex sympathetic dystrophy and causalgia. It describes a number of neurological and related symptoms which typically occur following surgery or a minor injury. CRPS is 3 times more common in women.

There are two types of CRPS:

- type I (most common): there is no demonstrable lesion to a major nerve
- type II: there is a lesion to a major nerve

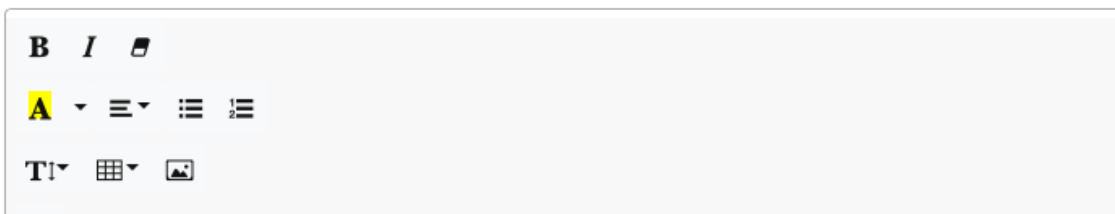
Features

- progressive, disproportionate symptoms to the original injury/surgery
- allodynia
- temperature and skin colour changes
- oedema and sweating
- motor dysfunction
- the Budapest Diagnostic Criteria are commonly used in the UK

Management

- early physiotherapy is important
- neuropathic analgesia in-line with NICE guidelines
- specialist management (e.g. Pain team) is required

Next question >



5-HT3 antagonists

5-HT3 antagonists are antiemetics used mainly in the management of chemotherapy related nausea. They mainly act in the chemoreceptor trigger zone area of the medulla oblongata.

Examples

- ondansetron
- granisetron

Adverse effects

- constipation is common

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Close

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Score f

2 in a row correct

Key facts from this session are shown below (score/attempts), click on the fact for background information

Ondansetron - 5-HT3 antagonist

[Notes](#) (1/1)

Phenytoin may cause dizziness

[Notes](#) (1/1)

Von Hippel-Lindau syndrome - chromosome 3

[Notes](#) (0/1)

Neck lumps

The table below gives characteristic exam question features for conditions causing neck lumps:

Condition	Notes
Reactive lymphadenopathy	By far the most common cause of neck swellings. There may be a history of local infection or a generalised viral illness
Lymphoma	Rubbery, painless lymphadenopathy The phenomenon of pain whilst drinking alcohol is very uncommon There may be associated night sweats and splenomegaly
Thyroid swelling	May be hypo-, eu- or hyperthyroid symptomatically Moves upwards on swallowing
Thyroglossal cyst	More common in patients < 20 years old Usually midline, between the isthmus of the thyroid and the hyoid bone Moves upwards with protrusion of the tongue May be painful if infected
Pharyngeal pouch	More common in older men Represents a posteromedial herniation between thyropharyngeus and cricopharyngeus muscles Usually not seen but if large then a midline lump in the neck that gurgles on palpation Typical symptoms are dysphagia, regurgitation, aspiration and chronic cough
Cystic hygroma	A congenital lymphatic lesion (lymphangioma) typically found in the neck, classically on the left side Most are evident at birth, around 90% present before 2 years of age
Branchial cyst	An oval, mobile cystic mass that develops between the sternocleidomastoid muscle and the pharynx Develop due to failure of obliteration of the second branchial cleft in embryonic development Usually present in early adulthood
Cervical rib	More common in adult females Around 10% develop thoracic outlet syndrome

Question 16

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Thyroglossal cyst

The key to understanding thyroglossal cysts is to think about the name; thyro (thyroid) and glossal (tongue).

Embryology

The thyroid develops from the floor of the pharynx and descends into the neck during its development. It is connected to the tongue by the thyroglossal duct. The foramen cecum is the point of attachment of the thyroglossal duct to the tongue. The thyroglossal duct normally atrophies but in some people may persist and give rise to a thyroglossal duct cyst.

Presentations

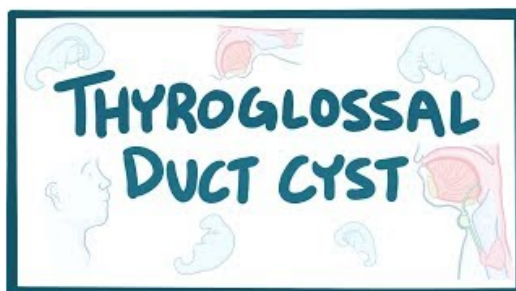
More common in patients < 20 years old.

Features

- usually midline, between the isthmus of the thyroid and the hyoid bone
- moves upwards with protrusion of the tongue
- may be painful if infected



Save my notes



Thyroglossal duct cyst

Headache

Headache accounts for a large proportion of medical consultations. The table below summarises the main characteristics of common or important causes:

Migraine	Recurrent, severe headache which is usually unilateral and throbbing in nature May be associated with aura, nausea and photosensitivity Aggravated by, or causes avoidance of, routine activities of daily living. Patients often describe 'going to bed'. In women may be associated with menstruation
Tension headache	Recurrent, non-disabling, bilateral headache, often described as a 'tight-band' Not aggravated by routine activities of daily living
Cluster headache*	Pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours with clusters typically lasting 4-12 weeks Intense pain around one eye (recurrent attacks 'always' affect same side) Patient is restless during an attack Accompanied by redness, lacrimation, lid swelling More common in men and smokers
Temporal arteritis	Typically patient > 60 years old Usually rapid onset (e.g. < 1 month) of unilateral headache Jaw claudication (65%) Tender, palpable temporal artery Raised ESR
Medication overuse headache	Present for 15 days or more per month Developed or worsened whilst taking regular symptomatic medication Patients using opioids and triptans are at most risk May be psychiatric co-morbidity

Other causes of headache

Acute single episode

- meningitis
- encephalitis
- subarachnoid haemorrhage
- head injury
- sinusitis

	Not aggravated by routine activities of daily living
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Other causes of headache

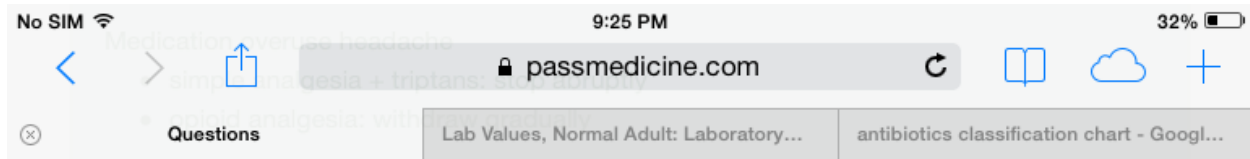
Acute single episode

- meningitis
- encephalitis
- subarachnoid haemorrhage
- head injury
- sinusitis
- glaucoma (acute closed-angle)
- tropical illness e.g. Malaria

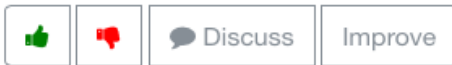
Chronic headache

- chronically raised ICP
- Paget's disease
- psychological

*some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin



This answer may seem counterintuitive but it is line with recent guidelines from SIGN, please see the link provided.



Next question >

Medication overuse headache

Medication overuse headache is one of the most common causes of chronic daily headache. It may affect up to 1 in 50 people

Features

- present for 15 days or more per month
- developed or worsened whilst taking regular symptomatic medication
- patients using opioids and triptans are at most risk
- may be psychiatric co-morbidity

Management (from 2008 SIGN guidelines)

- simple analgesics and triptans should be withdrawn abruptly (may initially worsen headaches)
- opioid analgesics should be gradually withdrawn

Next question >



Cluster headache

Cluster headaches are known to be one of the most painful conditions that patients can have the misfortune to suffer. The name relates to the pattern of the headaches - they typically occur in clusters lasting several weeks, with the clusters themselves typically once a year.

Cluster headaches are more common in men (3:1) and smokers. Alcohol may trigger an attack and there also appears to be a relation to nocturnal sleep.

Features

- pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours
- clusters typically last 4-12 weeks
- intense sharp, stabbing pain around one eye (recurrent attacks 'always' affect same side)
- patient is restless and agitated during an attack
- accompanied by redness, lacrimation, lid swelling
- nasal stuffiness
- miosis and ptosis in a minority

Management

- acute: 100% oxygen (80% response rate within 15 minutes), subcutaneous triptan (75% response rate within 15 minutes)
- prophylaxis: verapamil is the drug of choice. There is also some evidence to support a tapering dose of prednisolone
- NICE recommend seeking specialist advice from a neurologist if a patient develops cluster headaches with respect to neuroimaging

Some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin

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Migraine: diagnostic criteria

The International Headache Society has produced the following diagnostic criteria for migraine without aura:

Point	Criteria
A	At least 5 attacks fulfilling criteria B-D
B	Headache attacks lasting 4-72 hours* (untreated or unsuccessfully treated)
C	Headache has at least two of the following characteristics: 1. unilateral location* 2. pulsating quality (i.e., varying with the heartbeat) 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
D	During headache at least one of the following: 1. nausea and/or vomiting* 2. photophobia and phonophobia
E	Not attributed to another disorder (history and examination do not suggest a secondary headache disorder or, if they do, it is ruled out by appropriate investigations or headache attacks do not occur for the first time in close temporal relation to the other disorder)

*In children, attacks may be shorter-lasting, headache is more commonly bilateral, and gastrointestinal disturbance is more prominent.

Migraine with aura (seen in around 25% of migraine patients) tends to be easier to diagnose with a typical aura being progressive in nature and may occur hours prior to the headache. Typical aura include a transient hemianopic disturbance or a spreading scintillating scotoma ('jagged crescent'). Sensory symptoms may also occur

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If we compare these guidelines to the **NICE criteria** the following points are noted:

- NICE suggests migraines may be unilateral or bilateral
- NICE also give more detail about typical auras:

Auras may occur with or without headache and:

- are fully reversible
- develop over at least 5 minutes
- last 5-60 minutes

The following aura symptoms are atypical and may prompt further investigation/referral;

- motor weakness
- double vision
- visual symptoms affecting only one eye
- poor balance
- decreased level of consciousness.

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Migraine: pregnancy, contraception and other hormonal factors

SIGN produced guidelines in 2008 on the management of migraine, the following is selected highlights:

Migraine during pregnancy

- paracetamol 1g is first-line
- aspirin 300mg or ibuprofen 400mg can be used second-line in the first and second trimester

Migraine and the combined oral contraceptive (COC) pill

- if patients have migraine with aura then the COC is absolutely contraindicated due to an increased risk of stroke (relative risk 8.72)

Migraine and menstruation

- many women find that the frequency and severity of migraines increase around the time of menstruation
- SIGN recommends that women are treated with mefenamic acid or a combination of aspirin, paracetamol and caffeine. Triptans are also recommended in the acute situation

Migraine and hormone replacement therapy (HRT)

- safe to prescribe HRT for patients with a history of migraine but it may make migraines worse

Next question >

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*caution should be exercised with young patients as acute dystonic reactions may develop

A screenshot of the Notepad application's toolbar. The toolbar contains buttons for Bold (B), Italic (I), Underline (U), a text color selector (currently set to yellow), bulleted list, numbered list, decrease indent, text alignment (Left, Center, Right, Justify), a grid icon, an image icon, and a link icon. Below the toolbar is a text area with the text "Save my notes" and a "Save my notes" button.

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Triptans

Triptans are specific 5-HT₁ agonists used in the acute treatment of migraine. They are generally used first-line in combination therapy with an NSAID or paracetamol.

Prescribing points

- should be taken as soon as possible after the onset of headache, rather than at onset of aura
- oral, orodispersible, nasal spray and subcutaneous injections are available

Adverse effects

- 'triptan sensations' - tingling, heat, tightness (e.g. throat and chest), heaviness, pressure

Contraindications

- patients with a history of, or significant risk factors for, ischaemic heart disease or cerebrovascular disease

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Clinical Knowledge Summaries ↑ 0 ↓ 1

[Migraine guidelines](#)

Close

Neuropathic pain

Neuropathic pain may be defined as pain which arises following damage or disruption of the nervous system. It is often difficult to treat and responds poorly to standard analgesia.

Examples include:

- diabetic neuropathy
- post-herpetic neuralgia
- trigeminal neuralgia
- prolapsed intervertebral disc

NICE updated their guidance on the management of neuropathic pain in 2013:

- first-line treatment*: amitriptyline, duloxetine, gabapentin or pregabalin
- if the first-line drug treatment does not work try one of the other 3 drugs
- tramadol may be used as 'rescue therapy' for exacerbations of neuropathic pain
- topical capsaicin may be used for localised neuropathic pain (e.g. post-herpetic neuralgia)
- pain management clinics may be useful in patients with resistant problems

*please note that for some specific conditions the guidance may vary. For example carbamazepine is used first-line for trigeminal neuralgia

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[2013 Neuropathic pain guidelines](#)

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Epileps

- carbamazepine is first-line
- failure to respond to treatment or atypical features (e.g. < 50 years old) should prompt referral to neurology

Key fact

Trigeminal Neuralgia guidelines

Selegili

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Next question >

Paraneoplastic syndromes affecting nervous system

Lambert-Eaton myasthenic syndrome

- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

Anti-Hu

- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

Anti-Yo

- associated with ovarian and breast cancer
- cerebellar syndrome

Anti-GAD antibody

- associated with breast, colorectal and small cell lung carcinoma
- stiff person's syndrome or diffuse hypertonia

Anti-Ri

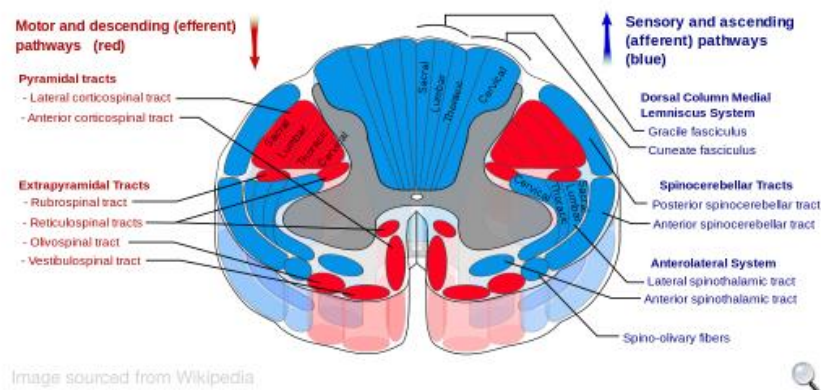
- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

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Spinal cord lesions

The diagram belows shows cross-section view of the spinal cord:



Motor lesions

Amyotrophic lateral sclerosis (motor neuron disease)

- affects both upper (corticospinal tracts) and lower motor neurons
- results in a combination of upper and lower motor neuron signs

Poliomyelitis

- affects anterior horns resulting in lower motor neuron signs

Combined motor and sensory lesions

Disorder	Tracts affected	Clinical notes
Brown-Sequard syndrome (spinal cord hemisection)	1. Lateral corticospinal tract 2. Dorsal columns 3. Lateral spinothalamic tract	1. Ipsilateral spastic paresis below lesion 2. Ipsilateral loss of proprioception and vibration sensation 3. Contralateral loss of pain and temperature sensation
Subacute combined degeneration of the spinal cord (vitamin B12 & E deficiency)	1. Lateral corticospinal tracts 2. Dorsal columns 3. Spinocerebellar tracts	1. Bilateral spastic paresis 2. Bilateral loss of proprioception and vibration sensation 3. Bilateral limb ataxia
Friedrich's ataxia	Same as subacute combined degeneration of the spinal cord	Same as subacute combined degeneration of the spinal cord

Combined motor and sensory lesions

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Friedrich's ataxia	Same as subacute combined degeneration of the spinal cord (see above)	Same as subacute combined degeneration of the spinal cord (see above) In addition cerebellar ataxia → other features e.g. intention tremor
Anterior spinal artery occlusion	1. Lateral corticospinal tracts 2. Lateral spinothalamic tracts	1. Bilateral spastic paresis 2. Bilateral loss of pain and temperature sensation
Syringomyelia	1. Ventral horns 2. Lateral spinothalamic tract	1. Flacid paresis (typically affecting the intrinsic hand muscles) 2. Loss of pain and temperature sensation
Multiple sclerosis	Asymmetrical, varying spinal tracts involved	Combination of motor, sensory and ataxia symptoms

Sensory lesions

Disorder	Tracts affected	Clinical notes
Neurosyphilis (tabes dorsalis)	1. Dorsal columns	1. Loss of proprioception and vibration sensation

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- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

Frontal lobes lesions

- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus. Speech is non-fluent, laboured, and halting
- disinhibition
- perseveration
- anosmia
- inability to generate a list

Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysdiadokinesis, nystagmus

More specific areas

Area	Associated conditions
Medial thalamus and mammillary bodies of the hypothalamus	Wernicke and Korsakoff syndrome
Subthalamic nucleus of the basal ganglia	Hemiballism
Striatum (caudate nucleus) of the basal ganglia	Huntington chorea
Substantia nigra of the basal ganglia	Parkinson's disease
Amygdala	Kluver-Bucy syndrome (hypersexuality, hyperorality, hyperphagia, visual agnosia)

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Lateral medullary syndrome



Lateral medullary syndrome, also known as Wallenberg's syndrome, occurs following occlusion of the posterior inferior cerebellar artery

Cerebellar features

- ataxia
- nystagmus

Brainstem features

- ipsilateral: dysphagia, facial numbness, cranial nerve palsy e.g. Horner's
- contralateral: limb sensory loss



Syringomyelia



Overview

- development of cavity (syrinx) within the spinal cord
- if extends into medulla then termed syringobulbia
- strongly associated with the Arnold-Chiari malformation

Features

- maybe asymmetrical initially
- slowly progressive, possibly over years
- motor: wasting and weakness of arms
- sensory: spinothalamic sensory loss (pain and temperature)
- loss of reflexes, bilateral upgoing plantars
- also seen: Horner's syndrome



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Degenerative cervical myelopathy

Degenerative cervical myelopathy (DCM) has a number of risk factors, which include smoking due to its effects on the intervertebral discs, genetics and occupation - those exposing patients to high axial loading [1].

The presentation of DCM is very variable. Early symptoms are often subtle and can vary in severity day to day, making the disease difficult to detect initially. However as a progressive condition, worsening, deteriorating or new symptoms should be a warning sign.

DCM symptoms can include any combination of [1]:

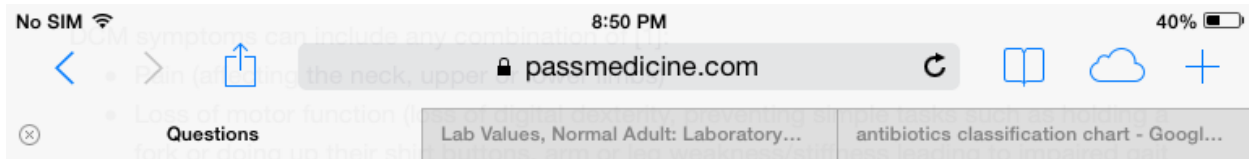
- Pain (affecting the neck, upper or lower limbs)
- Loss of motor function (loss of digital dexterity, preventing simple tasks such as holding a fork or doing up their shirt buttons, arm or leg weakness/stiffness leading to impaired gait and imbalance)
- Loss of sensory function causing numbness
- Loss of autonomic function (urinary or faecal incontinence and/or impotence) - these can occur and do not necessarily suggest cauda equina syndrome in the absence of other hallmarks of that condition

The most common symptoms at presentation of DCM are unknown, but in one series 50% of patients were initially incorrectly diagnosed and sometimes treated for carpal tunnel syndrome [2].

An MRI of the cervical spine is the gold standard test where cervical myelopathy is suspected. It may reveal disc degeneration and ligament hypertrophy, with accompanying cord signal change.

All patients with degenerative cervical myelopathy should be urgently referred for assessment by specialist spinal services (neurosurgery or orthopaedic spinal surgery). This is due to the importance of early treatment. The timing of surgery is important, as any existing spinal cord damage can be permanent. Early treatment (within 6 months of diagnosis) offers the best chance of a full recovery but at present, most patients are presenting too late. In one study, patients averaged over 5 appointments before diagnosis, representing >2 years.

Currently, decompressive surgery is the only effective treatment. It has been shown to prevent



- and imbalance
- Loss of sensory function causing numbness
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Currently, decompressive surgery is the only effective treatment. It has been shown to prevent disease progression. Close observation is an option for mild stable disease, but anything progressive or more severe requires surgery to prevent further deterioration. Physiotherapy should only be initiated by specialist services, as manipulation can cause more spinal cord damage.

References

1. Baron EM, Young WF. Cervical spondylotic myelopathy: a brief review of its pathophysiology, clinical course, and diagnosis. *Neurosurgery*. 2007 Jan;60(1 Suppl 1):S35-41.
2. Behrbalk E, Salame K, Regev GJ, Keynan O, Boszczyk B, Lidar Z. Delayed diagnosis of cervical spondylotic myelopathy by primary care physicians. *Neurosurg Focus*. 2013 Jul;35(1):E1.

Next question >

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Mobile browser interface showing the URL **passmedicine.com**. The top status bar displays "No SIM", signal strength, time "10:07 PM", and battery level "61%". The browser's address bar includes navigation icons, a search icon, and a "+" icon. Below the address bar, there are tabs for "Questions", "Lab Values, Normal Adult: Laboratory...", and "antibiotics classification chart - Googl...". A blue button labeled "Next question >" is positioned to the right of the tabs.

Foot drop

Foot drop is a result of weakness of the foot dorsiflexors.

Possible causes include:

- L5 radiculopathy
- sciatic nerve lesion
- common peroneal nerve lesion
- superficial or deep peroneal nerve lesion
- other possible includes central nerve lesions (e.g. stroke) but other features are usually present

A **common peroneal nerve lesion is the most common cause**. This is often secondary to compression at the neck of the fibula. This may be caused by certain positions such as leg crossing, squatting or kneeling. Prolonged confinement, recent weight loss, Baker's cysts and plaster casts to the lower leg are also known to be precipitating factors.

Examination

- if the patient has an isolated peroneal neuropathy there will be weakness of foot dorsiflexion and eversion. Reflexes will be normal
- weakness of hip abduction is suggestive of a L5 radiculopathy

Bilateral symptoms, fasciculations or other abnormal neurological findings (e.g. hyperreflexia) are indications for specialist referral.

If the examination suggests a peroneal neuropathy then conservative management is appropriate. Leg crossing, squatting and kneeling should be avoided. Symptoms typically improve over 2-3 months.*

*BMJ 2015;350:h1736 - Foot drop

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Vasculitis 35%

The other causes are associated with a demyelinating pathology



Next question >

Peripheral neuropathy: demyelinating vs. axonal

Demyelinating pathology

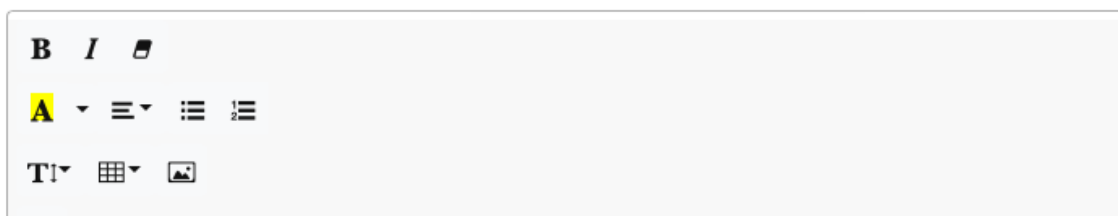
- Guillain-Barre syndrome
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- amiodarone
- hereditary sensorimotor neuropathies (HSMN) type I
- paraprotein neuropathy

Axonal pathology

- alcohol
- diabetes mellitus*
- vasculitis
- vitamin B12 deficiency*
- hereditary sensorimotor neuropathies (HSMN) type II

* may also cause a demyelinating picture

Next question >



Next question >

Post-lumbar puncture headache

Headache following lumbar puncture (LP) occurs in approximately one-third of patients. The pathophysiology of is unclear but may relate to a 'leak' of CSF following dural puncture. Post-LP headaches are more common in young females with a low body mass index

Typical features

- usually develops within 24-48 hours following LP but may occur up to one week later
- may last several days
- worsens with upright position
- improves with recumbent position

Factors which may contribute to headache	Factors which do not contribute to headache
Increased needle size Direction of bevel Not replacing the stylet Increased number of LP attempts	Increased volume of CSF removed Bed rest following procedure Increased fluid intake post procedure Opening pressure of CSF Position of patient

Management

- supportive initially (analgesia, rest)
- if pain continues for more than 72 hours then specific treatment is indicated, to prevent subdural haematoma
- treatment options include: blood patch, epidural saline and intravenous caffeine

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Cerebrospinal fluid: raised protein

Normal values of cerebrospinal fluid (CSF) are as follows:

- pressure = 60-150 mm (patient recumbent)
- protein = 0.2-0.4 g/l
- glucose = $> 2/3$ blood glucose
- cells: red cells = 0, white cells $< 5/\text{mm}^3$

The following conditions are associated with raised protein levels

- Guillain-Barre syndrome
- tuberculous, fungal and bacterial meningitis
- Froin's syndrome*
- viral encephalitis

*describes an increase in CSF protein below a spinal canal blockage (e.g. tumour, disc, infection)



Cerebrospinal fluid: raised lymphocytes

Normal values of cerebrospinal fluid (CSF) are as follows:

- pressure = 60-150 mm (patient recumbent)
- protein = 0.2-0.4 g/l
- glucose = $> 2/3$ blood glucose
- cells: red cells = 0, white cells $< 5/\text{mm}^3$

The following conditions are associated with raised lymphocytes

- viral meningitis/encephalitis
- TB meningitis
- partially treated bacterial meningitis
- Lyme disease
- Behcet's, SLE
- lymphoma, leukaemia



Next question >

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

Features

- headache
- blurred vision
- papilloedema (usually present)
- enlarged blind spot
- sixth nerve palsy may be present

Risk factors

- obesity
- female sex
- pregnancy
- drugs*: oral contraceptive pill, steroids, tetracycline, vitamin A, lithium

Management

- weight loss
- diuretics e.g. acetazolamide
- topiramate is also used, and has the added benefit of causing weight loss in most patients
- repeated lumbar puncture
- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure

*if intracranial hypertension is thought to occur secondary to a known causes (e.g. Medication) then it is of course not idiopathic

Next question >

Acute disseminated encephalomyelitis

Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease of the central nervous system. It may also be termed post infectious encephalomyelitis. The aetiology is not fully understood and it can occur following infection with a bacterial or viral pathogen. Common infections include measles, mumps, rubella, varicella and small pox, however this list is not exhaustive.

After a lag time of between a few days to 2 months there is an acute onset of multifocal neurological symptoms with rapid deterioration. Non-specific signs such as headache, fever, nausea and vomiting may also accompany the onset of illness. Motor and sensory deficits are frequent and there may also be brainstem involvement including oculomotor defects.

There are no specific biomarkers for the diagnosis of ADEM. MRI imaging may show areas of supra and infra-tentorial demyelination. Management involves intravenous glucocorticoids and the consideration of IVIG where this fails.

[Next question >](#)

Brain abscess

- CNS abscesses may result from a number of causes including, extension of sepsis from middle ear or sinuses, trauma or surgery to the scalp, penetrating head injuries and embolic events from endocarditis.

- The presenting symptoms will depend upon the site of the abscess (those in critical areas e.g. motor cortex) will present earlier. Abscesses have a considerable mass effect in the brain and raised intra cranial pressure is common.
- Although fever, headache and focal neurology are highly suggestive of a brain abscess the absence of one or more of these does not exclude the diagnosis, fever may be absent and even if present, is usually not the swinging pyrexia seen with abscesses at other sites.
- Assessment of the patient includes imaging with CT scanning.
- Treatment is usually surgical, a craniotomy is performed and the abscess cavity debrided. The abscess may reform because the head is closed following abscess drainage.

[Next question >](#)

Herpes simplex encephalitis

Herpes simplex (HSV) encephalitis is a common topic in the exam. The virus characteristically affects the temporal lobes - questions may give the result of imaging or describe temporal lobe signs e.g. aphasia

Features

- fever, headache, psychiatric symptoms, seizures, vomiting
- focal features e.g. aphasia
- peripheral lesions (e.g. cold sores) have no relation to presence of HSV encephalitis

Pathophysiology

- HSV-1 responsible for 95% of cases in adults
- typically affects temporal and inferior frontal lobes

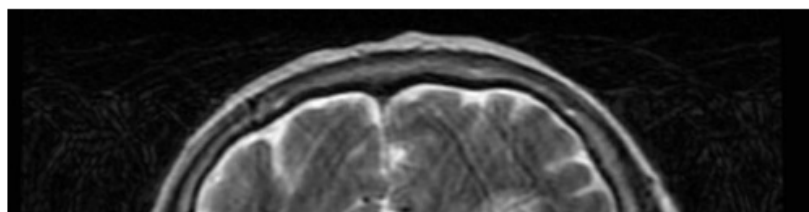
Investigation

- CSF: lymphocytosis, elevated protein
- PCR for HSV
- CT: medial temporal and inferior frontal changes (e.g. petechial haemorrhages) - normal in one-third of patients
- MRI is better
- EEG pattern: lateralised periodic discharges at 2 Hz

Treatment

- intravenous aciclovir

The prognosis is dependent on whether aciclovir is commenced early. If treatment is started promptly the mortality is 10-20%. Left untreated the mortality approaches 80%



Third nerve palsy

Features

- eye is deviated 'down and out'
- ptosis
- pupil may be dilated (sometimes called a 'surgical' third nerve palsy)

Causes

- diabetes mellitus
- vasculitis e.g. temporal arteritis, SLE
- false localizing sign* due to uncal herniation through tentorium if raised ICP
- posterior communicating artery aneurysm (pupil dilated)
- cavernous sinus thrombosis
- Weber's syndrome: ipsilateral third nerve palsy with contralateral hemiplegia -caused by midbrain strokes
- other possible causes: amyloid, multiple sclerosis

*this term is usually associated with sixth nerve palsies but it may be used for a variety of neurological presentations

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Fourth nerve palsy

Overview

- supplies superior oblique (depresses eye, moves inward)

Features

- vertical diplopia
- classically noticed when reading book or going down stairs

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Miosis

Causes of miosis (small pupil)

- Horner's syndrome
- Argyll-Robertson pupil
- senile miosis
- pontine haemorrhage
- congenital

Drugs causes

- opiates
- parasympathomimetics: pilocarpine
- organophosphate toxicity

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Nystagmus

Upbeat nystagmus

- cerebellar vermis lesions

Downbeat nystagmus - foramen magnum lesions

- Arnold-Chiari malformation



Image sourced from Wikipedia

Horizontal optokinetic nystagmus, a normal (physiological) form of nystagmus

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Facial nerve palsy

The facial nerve is the main nerve supplying the structures of the second embryonic branchial arch. It is predominantly an efferent nerve to the muscles of facial expression, digastric muscle and also to many glandular structures. It contains a few afferent fibres which originate in the cells of its genicular ganglion and are concerned with taste.

Supply - 'face, ear, taste, tear'

- face: muscles of facial expression
- ear: nerve to stapedius
- taste: supplies anterior two-thirds of tongue
- tear: parasympathetic fibres to lacrimal glands, also salivary glands

Causes of bilateral facial nerve palsy

- sarcoidosis
- Guillain-Barre syndrome
- Lyme disease
- bilateral acoustic neuromas (as in neurofibromatosis type 2)
- as Bell's palsy is relatively common it accounts for up to 25% of cases of bilateral palsy, but this represents only 1% of total Bell's palsy cases

Causes of unilateral facial nerve palsy - as above plus

Lower motor neuron

- Bell's palsy
- Ramsay-Hunt syndrome (due to herpes zoster)
- acoustic neuroma
- parotid tumours
- HIV
- multiple sclerosis*
- diabetes mellitus

Upper motor neuron

- stroke

LMN vs. UMN

- upper motor neuron lesion 'spares' upper face i.e. forehead
- lower motor neuron lesion affects all facial muscles

*may also cause an UMN palsy

Path

Subarachnoid path

- Origin: motor- pons, sensory- nervus intermedius
- Pass through the petrous temporal bone into the internal auditory meatus with the vestibulocochlear nerve. Here they combine to become the facial nerve.

Facial canal path

- The canal passes superior to the vestibule of the inner ear
- At the medial aspect of the middle ear, it becomes wider and contains the geniculate ganglion.

- 3 branches:

- 1. greater petrosal nerve
- 2. nerve to stapedius
- 3. chorda tympani

Stylomastoid foramen

- Passes through the stylomastoid foramen (tympanic cavity anterior and mastoid antrum posteriorly)
 - Posterior auricular nerve and branch to posterior belly of digastric and stylohyoid muscle
- 

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Bell's palsy

Bell's palsy may be defined as an acute, unilateral, idiopathic, facial nerve paralysis. The aetiology is unknown although the role of the herpes simplex virus has been investigated previously. The peak incidence is 20-40 years and the condition is more common in pregnant women.

Features

- lower motor neuron facial nerve palsy - forehead affected*
- patients may also notice post-auricular pain (may precede paralysis), altered taste, dry eyes, hyperacusis

Management

- in the past a variety of treatment options have been proposed including no treatment, prednisolone only and a combination of aciclovir and prednisolone
- following a National Institute for Health randomised controlled trial it is now recommended that prednisolone 1mg/kg for 10 days should be prescribed for patients within 72 hours of onset of Bell's palsy. Adding in aciclovir gives no additional benefit
- eye care is important - prescription of artificial tears and eye lubricants should be considered

Prognosis

- if untreated around 15% of patients have permanent moderate to severe weakness

*upper motor neuron lesion 'spares' upper face

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Ramsay Hunt syndrome

Ramsay Hunt syndrome (herpes zoster oticus) is caused by the reactivation of the varicella zoster virus in the geniculate ganglion of the seventh cranial nerve.

Features

- auricular pain is often the first feature
- facial nerve palsy
- vesicular rash around the ear
- other features include vertigo and tinnitus

Management

- oral aciclovir and corticosteroids are usually given

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Acute confusional state

Acute confusional state is also known as delirium or acute organic brain syndrome. It affects up to 30% of elderly patients admitted to hospital.

Features - wide variety of presentations

- memory disturbances (loss of short term > long term)
- may be very agitated or withdrawn
- disorientation
- mood change
- visual hallucinations
- disturbed sleep cycle
- poor attention

Management

- treatment of underlying cause
- modification of environment
- the 2006 Royal College of Physicians publication 'The prevention, diagnosis and management of delirium in older people: concise guidelines' recommended haloperidol 0.5 mg as the first-line sedative
- the 2010 NICE delirium guidelines advocate the use of haloperidol or olanzapine

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Neuroleptic malignant syndrome

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Neuroleptic malignant syndrome is a rare but dangerous condition seen in patients taking antipsychotic medication. It carries a mortality of up to 10% and can also occur with atypical antipsychotics. It may also occur with dopaminergic drugs (such as levodopa) for Parkinson's disease, usually when the drug is suddenly stopped or the dose reduced.

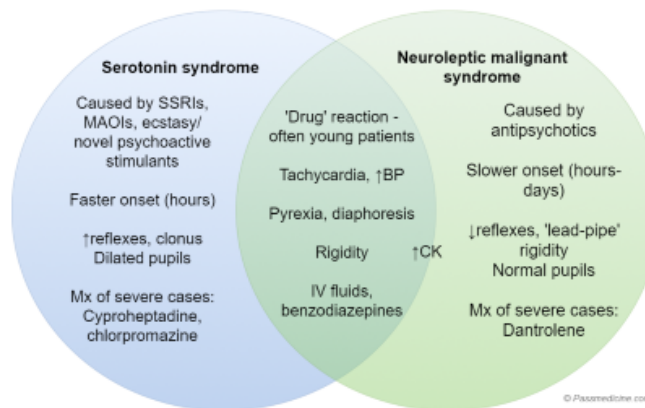
Features

- more common in young male patients
- onset usually in first 10 days of treatment or after increasing dose
- pyrexia
- rigidity
- tachycardia

A raised creatine kinase is present in most cases. A leukocytosis may also be seen

Management

- stop antipsychotic
- IV fluids to prevent renal failure
- dantrolene* may be useful in selected cases
- bromocriptine, dopamine agonist, may also be used



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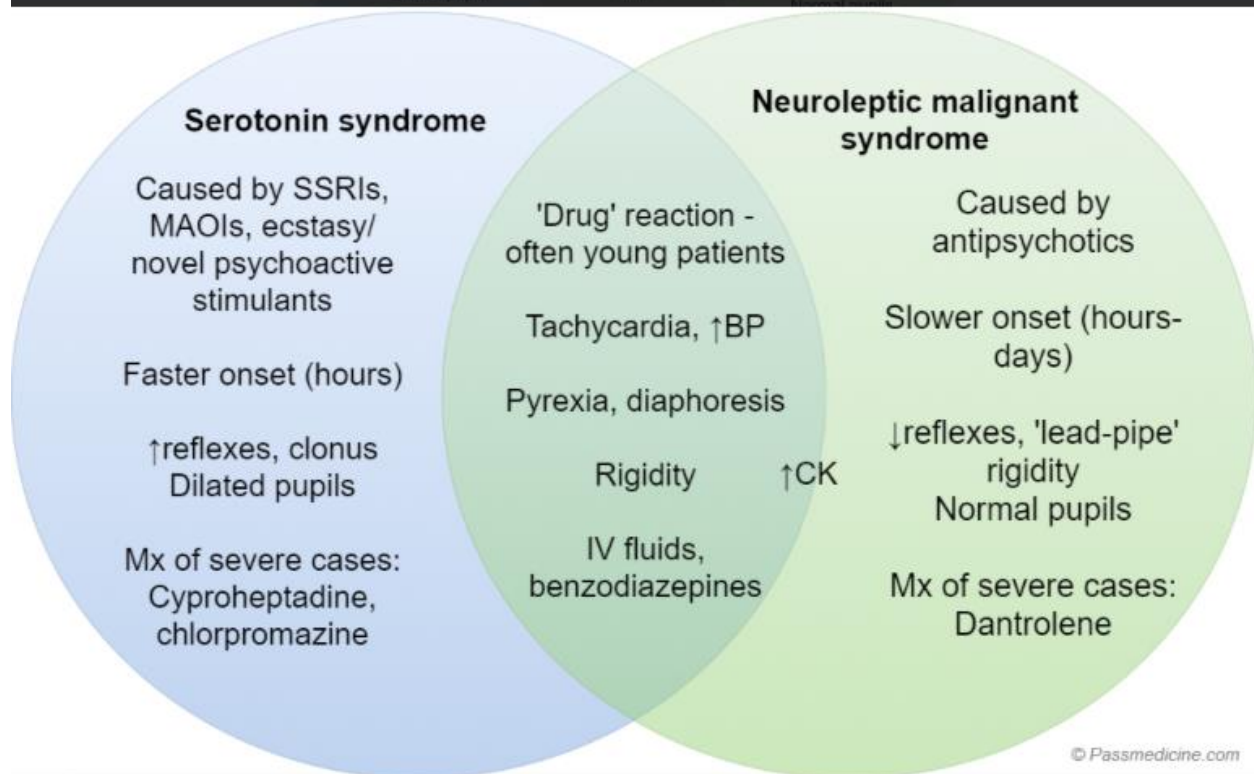


Venn diagram showing contrasting serotonin syndrome with neuroleptic malignant syndrome. Note that both conditions can cause a raised creatine kinase (CK) but it tends to be more associated with NMS.

*thought to work by decreasing excitation-contraction coupling in skeletal muscle by binding to the ryanodine receptor, and decreasing the release of calcium from the sarcoplasmic reticulum

- bromocriptine, dopamine agonist, may also be used

Serotonin syndrome	Neuroleptic malignant syndrome	
Caused by SSRIs, MAOIs, ecstasy/ novel psychoactive stimulants	'Drug' reaction - often young patients	Caused by antipsychotics
Faster onset (hours)	Tachycardia, ↑BP	Slower onset (hours-days)
↑reflexes, clonus, Dilated pupils	Pyrexia, diaphoresis	↓reflexes, 'lead-pipe' rigidity
	Rigidity	↑CK



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